

## **BLOOD ASSESSMENT OF INJURY**

### **RELATED APPLICATION**

This application claims priority under 35 U.S.C. §119 of U.S. Provisional  
5 Application Serial No. 60/253,568 filed November 28, 2000.

### **FIELD OF THE INVENTION**

The present invention is directed toward methods of assessing injury in an individual, wherein injury is defined as cell death, cell dysfunction, or genetic abnormalities either acquired or inherent, any of which are present in an occult, acute  
10 or chronic stage. More particularly, the invention is directed toward methods of injury assessment which comprise determining a pattern of expression exhibited by obtained blood cells and comparing the pattern of expression exhibited by the obtained blood cells to an injury database to assess the injury.

### **BACKGROUND OF THE INVENTION**

15 Non-invasive diagnostic methods such as computed tomography (CT) and magnetic resonance imaging (MRI) are useful in diagnosing injury resulting from ischemia, tumors, bleeding, trauma, toxins, infection, autoimmune disease and other etiologies. Invasive imaging methods include positron emission tomography (PET) and single photon emission computed tomography (SPECT), which require the  
20 injection of radioisotopes, and cerebral angiography and myelography, which require the injection of radiopaque dyes. A further invasive procedure for assessing injury is through the use of a biopsy.

many factors, including cardiac arrest, strokes, hemorrhages, hypoglycemia episodes, head injuries, seizures, psychiatric diseases, infection, toxins, drugs, as well as coma due to liver, renal, endocrine or pulmonary failure. Such patients may be unable to respond to requests regarding a medical history or conditions. Further, it is often  
5 difficult to transport or to use imaging technology on artificially ventilated patients in intensive care units or post-surgical units. Still further, it is complicated to perform a biopsy when the source or the cause of the injury may be unknown. Thus, it would be useful to have a convenient method of assessing injuries that does not require a biopsy, imaging or transfer of the patient, and can be done with procedures no more  
10 invasive than the withdrawal of a blood sample.

Neither CT nor MRI are useful for diagnosing injury where there is isolated dysfunction or isolated loss of neurons or individual cells in the blood, brain, spinal cord, lung, muscles, nerves or other organs. For example, there are no convenient methods for determining whether injury to cells in the brain, blood, muscle, nerves,  
15 heart, lung, endocrine glands or other organs has occurred following hypoglycemia, hypoxia, drug over-dose, coma, status epilepticus, stroke, or severe hypotension due to cardiac arrest or other causes. In addition, even with these imaging methods there are numerous injuries that cannot be conveniently or adequately assessed. For example, patients suffering cardiac arrest with cardiovascular collapse often have  
20 diffuse neuronal injury in the brain and in other organs that cannot be visualized. Similarly, injury caused by hypoxia, hypoglycemia, or status epilepticus cannot be diagnosed with such methods. Thus, it would be useful to have a convenient and adequate method to assess injury states.

Many individuals remain asymptomatic for an injury for numerous years. Such individuals do not seek medical treatment because the injury is not prevalent. In addition, such individuals cannot report an accurate medical history because they are not aware of a hidden medical condition. Therefore, it is nearly impossible to accurately assess injury in these individuals when symptoms are not overtly expressed. Thus, it would be useful to have a convenient method of assessing asymptomatic injuries to continuously monitor an individual's health.

The prior art teaches that specific genes or proteins have been identified that correspond with a particular specific disease. In addition, these genes and proteins can be classified using microarray technology. The identification and measurement of these specific genes and proteins allow a specific disease to be diagnosed.

For Example, Barone, et al., *J. Cereb. Blood Flow Metab.*, 19(8):819-834 (1999), teach that transforming growth factor (TGF), tissue necrosis factor (TNF), interleukin-1 (IL-1), interleukin-8 (IL-8), heat shock proteins, and metalloproteinases may be induced, for example, in the brain during a stroke. Bergeron et al., *European Journal of Neuroscience*, 11:4159-4170 (1999), teach that hypoxia-inducible factor-1 (HIF-1), glucose transporter-1 (GLUT-1), and several glycolytic enzymes are upregulated in, for example, the brain during focal ischemia. HIF-1 is induced by hypoxia, but not by hypoglycemia – making this gene a candidate for distinguishing between hypoxia and hypoglycemia in blood, the brain and other organs. Sharp et al., *TINS*, 22:97-99 (1999), teach that heat shock proteins (HSPs) and glucose-regulated proteins (GRPs) are produced in response to ischemia and other stresses. HSPs are induced in response to denatured proteins, GRPs are induced in response to low

glucose, and ORPs (oxygen regulated proteins) are induced in response to low oxygen. Martens et al., *Stroke*, 29:2363-2366 (1998), teach that S-100 protein, a calcium-binding protein, may be a serum marker of brain damage useful for clinical assessment. Martens et al. further teach that cardiac arrest may produce cerebral  
5 damage that can be detected by release of neuron-specific enolase to the cerebrospinal fluid and eventually to the blood.

Microarrays of DNA have been used to classify types of cancer, as taught by Alizadeh et al., *Nature*, 403:503-511 (2000), and Golub et al., *Science*, 283:531-537 (1999). Microarrays have also been used in analyzing inflammatory diseases such as  
10 rheumatoid arthritis and inflammatory bowel disease, as taught by Heller et al., *Proc. Natl. Acad. Sci., U.S.A.*, 94:2150-2155 (1997). Friend et al, (Rosetta Inpharmactics, Inc.) U.S. Patent No. 6,218,122 (2001), teach a method for monitoring disease states and levels of effect of therapies using gene expression profiles derived from cellular constituents indicating aspects of the biological state of the cell, such as RNA or  
15 protein abundances or activity levels. Erlander et al (Ortho-McNeil Pharmaceutical, Inc.) WO 00/28092 (2000), teach a method for the production of gene expression profiles from a selected set of cells residing in a given tissue/organ. Friend et al, (Rosetta Inpharmactics, Inc.) WO 00/24936 (2000), teach methods of using co-regulated genesets to enhance the detection and classification of specific gene  
20 expression patterns for a specific biological state. Ralph et al., (Urocor, Inc.) U.S. Patent No. 6,190,857 (2001), teach that a specific human disease state may be detected in circulating leukocytes by identifying specific genomic markers for the specific disease state.

However, even with the progression in the art, there remains a substantial need for convenient and adequate methods that can assess an injury for an individual. It would also be advantageous to provide methods of assessment which could be conveniently and adequately used in particular individuals who are asymptomatic, artificially ventilated and/or in altered states of consciousness, and that go beyond current methods of clinical diagnosis.

There is also a substantial need for methods of assessment that could utilize a relatively non-invasive procedure for diagnosis, prognosis, and/or monitoring an injury state.

## 10 SUMMARY OF THE INVENTION

Accordingly, it is an object of this invention to provide convenient methods of assessing injury.

In accordance with one aspect of the invention, there are provided methods of injury assessment in an individual. The methods comprise the steps of determining a pattern of expression exhibited by blood cells obtained from the individual and comparing the pattern of expression exhibited by the blood cells to an injury database to assess the injury. In specific embodiments, the pattern of expression may be a pattern of gene expression, protein expression, or combinations thereof, and the injury database may be a genomic database, proteomic database, or combinations thereof. Furthermore, the injury database may be based on a specific organ or a specific injury cause or disease.

In accordance with another aspect of the invention, there are provided methods of stroke injury assessment of an individual comprising the steps of obtaining a

peripheral blood sample from the individual, capturing a pattern of expression, defining a pattern of expression, and comparing the pattern of expression exhibited by the blood cells to an injury database to assess stroke injury.

In accordance with yet another aspect of the invention, there are provided  
5 methods of hypoxia injury assessment of an individual comprising the steps of obtaining a peripheral blood sample from the individual, capturing a pattern of expression, defining a pattern of expression, and comparing the pattern of expression exhibited by the blood cells to an injury databases to assess hypoxia injury.

In accordance with a further aspect of the invention, there are provided  
10 methods of hypoglycemia injury assessment of an individual comprising the steps of obtaining a peripheral blood sample from the individual, capturing a pattern of expression, defining a pattern of expression, and comparing the pattern of expression exhibited by the blood cells to an injury bank to assess hypoglycemia injury.

In accordance with yet another aspect of the invention, there are provided  
15 methods of seizure injury assessment of an individual comprising the steps of obtaining a peripheral blood sample from the individual, capturing a pattern of expression, defining a pattern of expression, and comparing the pattern of expression exhibited by the blood cells to an injury database to assess seizure injury.

In accordance with yet another aspect of the invention, there are provided  
20 methods of movement disorder injury assessment of an individual comprising the steps of obtaining a peripheral blood sample from the individual, capturing a pattern of expression, defining a pattern of expression, and comparing the pattern of

expression exhibited by the blood cells to an injury database to assess movement disorder injury.

In accordance with yet another aspect of the invention, there are provided methods of diabetes injury assessment of an individual comprising the steps of  
5 obtaining a peripheral blood sample from the individual, capturing a pattern of expression, defining a pattern of expression, and comparing the pattern of expression exhibited by the blood cells to an injury database to assess diabetes injury.

In accordance with yet another aspect of the invention, there are provided methods of infectious disease assessment of an individual comprising the steps of  
10 obtaining a peripheral blood sample from the individual, capturing a pattern of expression, defining a pattern of expression, and comparing the pattern of expression exhibited by the blood cells to an injury database to assess infectious disease injury.

In accordance with yet another aspect of the invention, there are provided methods of immune mediated disease assessment of an individual comprising the  
15 steps of obtaining a peripheral blood sample from the individual, capturing a pattern of expression, defining a pattern of expression, and comparing the pattern of expression exhibited by the blood cells to an injury database to assess immune mediated disease injury.

In accordance with yet another aspect of the invention, there are provided  
20 methods of efficacy or toxicity assessment, or combinations thereof, of an individual comprising the steps of obtaining a peripheral blood sample from the individual, capturing a pattern of expression, defining a pattern of expression, and comparing the pattern of expression exhibited by the blood cells to an injury database to assess

efficacy or toxicity, or combinations thereof. The methods can be used, for example, for assessing efficacy and/or toxicity of drugs or environmental toxins.

In accordance with yet another aspect of the invention, there are provided methods of psychosis assessment, or combinations thereof, of an individual  
5 comprising the steps of obtaining a peripheral blood sample from the individual, capturing a pattern of expression, defining a pattern of expression, and comparing the pattern of expression exhibited by the blood cells to an injury database to assess psychosis.

In accordance with yet another aspect of the invention, there are provided  
10 methods of headache assessment, or combinations thereof, of an individual comprising the steps of obtaining a peripheral blood sample from the individual, capturing a pattern of expression, defining a pattern of expression, and comparing the pattern of expression exhibited by the blood cells to an injury database to assess headache.

In accordance with yet another aspect of the invention, there are provided  
15 methods of genetic disorder assessment, or combinations thereof, of an individual comprising the steps of obtaining a peripheral blood sample from the individual, capturing a pattern of expression, defining a pattern of expression, and comparing the pattern of expression exhibited by the blood cells to an injury database to assess the  
20 genetic disorder.

In accordance with yet another aspect of the invention, there are provided methods of proliferative disease assessment, or combinations thereof, of an individual comprising the steps of obtaining a peripheral blood sample from the individual,

capturing a pattern of expression, defining a pattern of expression, and comparing the pattern of expression exhibited by the blood cells to an injury database to assess the proliferative disease disorder.

The present methods are advantageous in providing convenient, relatively non-invasive diagnosis of injury in occult, acute or chronic stages. Additional embodiments, objects and advantages of the invention will become more fully apparent in view of the following description.

### **BRIEF DESCRIPTION OF THE DRAWINGS**

The following detailed description will be more fully understood in view of the drawings in which:

Figure 1a is a Venn diagram showing the numbers of genes that were upregulated more than twofold in blood 24 hours after brain ischemia (BI), brain hemorrhage (BH), and sham surgery (S), compared with untouched control individuals, as described in Example 2;

Figure 1b is a Venn diagram showing the numbers of genes that were downregulated more than twofold in blood 24 hours after kainate (K), insulin-glucose (IG), and hypoxia (H), compared with untouched control individuals, as described in Example 2;

Figure 2 is a cluster analysis of the pattern of expression obtained from individuals with kainate, insulin-glucose, hypoxia, brain ischemia, brain hemorrhage, as compared to sham surgery and untouched control individuals, as described in the Example 2;

Figure 3a is a graph which demonstrates the identification of Dead Box Y Isoform, which is differentially expressed in two groups of patients, males and females, as described in Example 3;

Figure 3b is a graph which demonstrates the identification of Ribosomal Protein S4 Y Isoform, which is differentially expressed in two groups of patients, males and females, as described in Example 3;

Figure 4 is a graph which demonstrates that genes SEQ ID NO:1 and SEQ ID NO:2 are expressed more highly in Parkinson's individuals as compared to other individuals without Parkinson's, as described in Example 4;

Figure 5 is a cluster analysis of the expression obtained from pediatric epilepsy patients prior to being treated compared to the expression of these individuals after being treated with anticonvulsant valporate (VPA) or the anticonvulsant carbamazepine (CPZ), as described in the Example 8;

Figure 6 is a cluster analysis of the pattern of expression obtained from individuals with neurofibromatosis, as described in Example 9;

Figure 7 is a cluster analysis of the pattern of expression obtained from individuals with bipolar, as described in Example 10;

Figure 8 is a cluster analysis of the pattern of expression obtained from individuals with acute migraine headaches, as described in Example 11;

Figure 9 is a cluster analysis of the pattern of expression obtained from individuals with schizophrenia, as described in the Example 12; and

Figure 10 is a cluster analysis of the pattern of expression obtained from individuals with Tourettes, as described in the Example 13.

## DETAILED DESCRIPTION

Upon injury, the blood, in particular the blood cells, will be exposed to environmental stresses, immune responses or additional effects associated with the injury. The inventors have found that blood cell responses can be used to determine whether there has been injury to neurons or injury to other cells in the body, the cause of the injury, and/or the degree of the injury. Methods in accordance with the invention may be used to detect remote injury. In addition, methods in accordance with the invention may be used to assess injury that cannot be conveniently or adequately evaluated by current blood tests, by imaging or biopsy, and may conveniently be used on all individuals, including individuals who are asymptomatic, in altered states of consciousness, and/or who are artificially ventilated. Advantageously, methods in accordance with the present invention are relatively non-invasive and do not require biopsy or the injection of radioisotopes or radiopaque dyes.

As used herein, "assessment" is intended to refer to the prognosis, diagnosis, or monitoring of an injury based upon a pattern of expression from a blood sample. As used herein, "individual", is intended to refer to an animal, including but not limited to humans, mammals, and rodents. As used herein "blood cells", is intended to refer to nucleated cells of the blood, including but not limited to red blood cells, white blood cells, lymphocytes, leukocytes, monocytes, macrophages, eosinophils, basophils, polymorphonuclear cells, all other subsets of cells containing RNA or protein, or combinations thereof.

As used herein, "injury" is intended to refer to genetic abnormalities, either inherent or acquired; death of cells; or dysfunction of cells produced by a wide variety of overt or covert states including, but not limited to, diffuse systemic disease, hyperproliferative cellular conditions, including benign, and non-benign or metastatic cancer, hemorrhage, infarction, ischemia, hypoxia, seizures, psychiatric illnesses, neurological diseases, hypoglycemia, trauma, toxins, drugs, organs, inflammatory diseases, autoimmune diseases, infectious diseases, demyelinating diseases, tumors, cancer, endocrine diseases, degenerative and metabolic diseases, including Alzheimer's, and infection, present in an occult, acute or chronic stage.

Autoimmune diseases include, but are not limited to, Graves, Rheumatoid arthritis, Thyroiditis/hypothyroidism, Vitiligo, IDDM, Multiple sclerosis, Primary glomerulonephritis, Systemic lupus erythematosus, Sjogren's, Addison's disease, autoimmune hemolytic anemia, chronic active hepatitis, Goodpasture's syndrome, idiopathic thrombocytopenia purpura, myasthenia gravis, myocarditis, pemphigus, pernicious anemia, polymyositis, primary biliary cirrhosis, relapsing polychondritis, rheumatic fever, scleroderma, and uveitis. Psychiatric illnesses include, but are not limited to, schizophrenia, generalized anxiety, panic disorders, post traumatic stress, obsessive compulsive, phobias, social anxiety disorder, major depressive disorder, bipolar, alcohol and drug abuse, and eating disorders.

As used herein, "organ injury" is meant to refer to injury to one or more organs, including but not limited to, the following: brain, organs of the special senses including eyes, ears and nose, the central nervous system, the spinal cord, nerves, muscles, heart, lung, kidney, liver, genitalia, endocrine glands, bladder,

gastrointestinal system, joints, bones, blood vessels, and blood cells, including red blood cells and white blood cells, and including lymphocytes, leukocytes, monocytes, macrophages, eosinophils, basophils, and all other cells found in blood.

As used herein, "glucose-inducible genes" is intended to refer to genes which  
5 are induced by changes in serum or blood glucose levels, usually low glucose levels, and decreased with high glucose levels; while "glucose-related proteins" is intended to refer to gene products which are produced or which levels are varied in response to changes in serum or blood glucose levels, preferably low glucose levels. "Low glucose levels" is intended to refer to glucose levels below the range generally  
10 regarded by physicians as normal. As used herein, "hypoxia-induced factors" is intended to refer to factors which are produced or which levels are varied in response to hypoxia.

As used herein, a "genomic injury bank" refers to a library composed of DNA, RNA, or combinations thereof, isolated from blood samples. As used herein, a  
15 "proteomic injury bank" refers to a library composed of protein isolated from blood samples. As used herein, an "injury database" refers to a database comprising a pattern of expression or patterns of expressions indicative of a single or different states of injury, including but not limited to pattern of gene expression, protein expression, or combinations thereof. The injury database may be based on a specific  
20 organ or a specific injury cause or disease. Organ specific injury databases include, but are not limited to, brain injury database, spinal cord injury database, blood injury database, muscle injury database, nerve injury database, lung injury database, liver injury database, heart injury database, kidney injury database, genitalia injury

database, eye injury database, ear injury database, nose injury database, teeth injury database, bone injury database, white blood cell injury database, endocrine gland injury database, gastrointestinal injury database, blood vessel injury database, or combinations thereof. Cause/disease specific injury databases include, but are not

5 limited to, global ischemic injury database, focal ischemic profile, status epilepticus injury database, hypoxia injury database, hypoglycemia injury database, cerebral hemorrhage injury database, hemorrhage injury database for one or more organs, diabetes complications injury database, psychosis injury database, psychiatric disease injury database, bipolar injury database, schizophrenia injury database, headache

10 injury database, acute migraine headache, database, endocrine disease injury database, uremia injury database, injury database for ammonemia with hepatic failure, toxin overdose injury database, drug overdose injury database, Alzheimer's disease injury database, Parkinson's disease injury database, Tourettes disease injury database, muscle disease injury database, proliferative disease injury database,

15 neurofibromatosis injury database, nerve disease injury database, other dementing illness injury database, inflammatory diseases injury database, autoimmune diseases injury database, infectious diseases injury database, demyelinating diseases injury database, trauma injury database, tumors injury database, cancer injury database, degenerative and metabolic diseases including Alzheimer's injury database, genetic or

20 familial diseases injury database, or combinations thereof.

As used herein "stroke" or "cerebrovascular accident" is intended to refer to cerebral infarction resulting from lack of blood flow and insufficient oxygen to the brain. As used herein, "infarction" is intended to refer to tissue/cell death. In an

ischemic stroke, the blood supply is cut off due to a blockage in a blood vessel, while in a hemorrhagic stroke the blood supply is cut off due to the bursting of a blood vessel.

As used herein, "pattern of expression" is meant to refer to the representation of molecules, including but not limited to genes, proteins or combinations thereof, in an injury state, which are upregulated, downregulated or embody no change. As used herein, "expression method" is meant to refer to any method known in the art that can define a pattern of expression, such as the significance analysis of microarrays and class prediction, as taught by Tusher, *Proceedings National Academy of Sciences*, 98: 5116 (2001). These methods may assess injury at a point minutes, hours, days or weeks after the injury has occurred, owing to rapid and/or prolonged expression of the molecules indicating the injury.

Patterns of expression may be derived from, but are not limited to, the following detailed injuries. For example, in individuals who sustain a brief period of severe hypoglycemia (low serum glucose) because of oral or injected hypoglycemics or because of severe illnesses there may be an induction of glucose-inducible genes in all of the blood cells, including polymorphonuclear cells (neutrophils), lymphocytes and macrophages. Hypoglycemia may also damage brain cells, blood cells, cells in the pancreas, cells in the heart, lung and other organs. Thus, gene and protein expression in the blood cells may change in response to the hypoglycemia.

In individuals who sustain a period of pure hypoxia during anesthesia or while on a respirator there may be an induction of a set of genes specific for hypoxia; therefore, glucose-inducible genes may not be induced. In contrast, in individuals

sustaining a cardiac arrest, wherein the brain, other organs and blood become ischemic for a length of time, there may be an induction of genes regulated by low glucose and low oxygen, as well as genes that are related to acidosis and ischemia. Thus, the genomic and/or proteomic response which may be observed in blood cells  
5 during episodes of pure hypoxia may differ from those observed in blood cells during episodes of pure hypoglycemia.

An individual having status epilepticus has brain injury manifested by isolated neuronal injury. The removal of such dead neurons is performed by monocytes and macrophages. Thus, during status epilepticus there may be selective change in  
10 genomic and/or proteomic expression of macrophages. Further, during repeated seizures there may be little white cell hypoxia or hypoglycemia, thus, hypoxia-induced factors, glucose-related proteins and heat shock proteins will not be induced. Additionally, during prolonged seizures there may be massive sympathetic discharge. The individuals may have elevation of catecholamines (e.g., epinephrine) that may  
15 stimulate adrenergic receptors in the blood cells.

If a individual is suffering from one or several focal strokes, blood cells respond to the site of the injury, the brain, and the response is targeted to brain antigens with removal and repair of neurons, glia, and vessels. During severe ischemic hypotension and infarction of the brain or other organs, hypoxia-induced  
20 factors, glucose-related proteins, and heat shock proteins are all induced. In heavy metal toxicity, heat shock proteins may be induced.

It has been found that molecules regulate in accordance with an injury state to determine a pattern of expression. In an embodiment of the invention, the number of

molecules necessary to define a pattern of expression is at lease about 10. In an embodiment of the invention, the number of molecules necessary to define a pattern of expression is at lease about 50. In a further embodiment of the invention, the number of molecules necessary to define a pattern of expression is at least about 200.

- 5 In a further embodiment of the invention, the number of molecules necessary to define a pattern of expression is at least about 500. In a further embodiment of the invention, the number of molecules necessary to define a pattern of expression is at least about 1000. In a further embodiment of the invention, the number of molecules necessary to define a pattern of expression is at least about 5000. In a further
- 10 embodiment of the invention, the number of molecules necessary to define a pattern of expression is about at least 10,000. In a further embodiment of the invention, the number of molecules necessary to define a pattern of expression is about at least 50,000. In a further embodiment of the invention, the number of molecules necessary to define a pattern of expression is about at least 100,000. In a further embodiment of
- 15 the invention, the number of molecules necessary to define a pattern of expression is all molecules represented in the injury state. The upper and/or lower limit of molecules necessary to define a pattern of expression may similarly vary in individuals applications of the present method, and in specific embodiments may be 10, 50, 200, 500, 1000, 5000, 10,000, 100,000, or the like.

- 20 In accordance with another embodiment of the invention, the molecules, which may be used in determining a pattern of expression by blood cells include, but are not limited to, intermediate metabolism, immune-related molecules, cytokines, chemokines, immediate early genes, structural genes, neurotransmitters, receptors,

signaling molecules, oncogenes and proto-oncogenes, heat shock and stress genes, transporters, trophic and growth factors, cell cycle genes, lipid metabolism, arachidonic acid metabolism, free radicals and free radical scavengers, metal binding, transporting genes, or combinations thereof.

5 In accordance with yet another embodiment of the invention, various enzymes whose expression may be evaluated comprise aldolase-A, lactase, dehydrogenase-A, phosphofructokinase-L, pyruvate kinase-M, hypoxia-inducible factor, or combinations thereof, while heat shock proteins whose gene expression may be evaluated comprise ubiquitin, HSP10, HSP27, HSP25, HSP32 (also known as heme  
10 oxygenase-1 or HO-1), HSP47, HSP60, HSC70 (also known as HSC73), HSP70 (also known as HSP72), HS90, HS100/105, or combinations thereof.

In accordance with a further embodiment of the invention, the classes of genes and proteins further comprise intermediate-early genes (IEGs), the genes for hypoxia-inducible factor 1 (HIF-1), glucose transporter-1 (GLUT-1), glycolytic enzymes,  
15 transforming growth factor (TGF), tissue necrosis factor (TNF), interleukin-1 (IL-1), interleukin-1 receptor antagonist (IL-1 RA), interleukin-8 (IL-8), heat shock proteins (HSPs), glucose-regulated proteins (GRPs), oxygen-regulated proteins, metalloproteinases, nitric oxide synthase (NOS), cyclooxygenases (COX), poly(ADP-ribose) polymerase (PARP), calcium-binding proteins such as S-100 proteins,  
20 histamine H2-receptor, c-jun leucine zipper interactive protein, Glut3, the vesicular monoamine transporter, TNF intracellular domain interacting protein, vascular tyrosine phosphatase, glucose-induced genes, hypoxia-induced genes, transcription factors, signaling factors, growth factors, transmitters, receptors, membrane protein

genes, peptides, cytokines, chemokines, structural genes, cell cycle genes, apoptosis-related genes, acidosis-induced genes, ischemia-induced genes, enzymes, kinases, phosphatases, trophic factors, nuclear factors, hormones, or combinations thereof.

Hypoxia-induced genes comprise genes for heat shock proteins, genes for nitric oxide

5 synthase, genes for matrix metalloproteinases, genes for cyclooxygenases, genes for growth factors, genes for hypoxia-induced factors such as HIF-1, and genes involved in the production of cytokines, chemokines, adhesion molecules, or combinations thereof. Glucose-induced genes comprise glucose regulated proteins, glycolytic enzymes, glycosylated proteins, genes as listed in Table 3, or combinations thereof.

10 Acidosis-induced genes comprise the genes as listed in Table 2, genes listed in Table 3, or combinations thereof. Ischemia-induced genes comprise the genes as listed in Table 3 or combinations thereof. Parkinson-related genes may comprise SEQ ID NO:1, SEQ ID NO:2, or combinations thereof.

The pattern of expression exhibited by the obtained blood cells may be  
15 captured by any method known to the art. An exemplary method is through the use of microarrays, for example using DNA microarrays, protein microarrays, peptide microarrays, or combinations thereof. Microarrays refer to surface microarrays, membrane microarrays, bead microarrays, solution microarrays, and the like comprised of nucleic acids, nucleic acid mimetics, discrete nucleotide sequences,  
20 preferably DNA or RNA sequences, discrete proteins, antibodies, protein fragments, antibody fragments, antibody-mimetics, peptides, peptide-mimetics, organic molecules and/or other molecules capable of selectively and specifically binding specific RNA, DNA or proteins; or subsets of RNA, DNA or protein molecules thus

permitting the detection and measurement of the associated molecules for the purpose of capturing a pattern of expression.

In one embodiment of the invention, microarrays are used to capture the pattern of gene expression. The nucleotide sequences in two DNA samples or two  
5 RNA samples, such as, for example, the RNA isolated from two different cell populations, are compared by first labeling the samples, mixing the samples and hybridizing them to arrayed DNA spots. Generally each nucleotide sequence is labeled with a different fluorescent dye or other labeling technique. As the samples are differentially labeled, it is possible to determine the pattern of gene expression.

10 To prepare RNA for use in a microarray assay, it is generally purified from total cellular content. Suitable methods of RNA isolation are known in the art and include the use of standard isolation methods, specific columns, or other collection methods. The RNA may be reversed transcribed to complementary DNA (cDNA) and in some applications to complementary RNA (cRNA). Either the labeled cDNA or  
15 the labeled cRNA may be used in the microarray assay.

Generally, the cDNA or cRNA samples are labeled, for example, with fluorescent dyes (fluors). Common fluors include Cy3 and Cy5. The labeled samples are referred to as probes. The probes are hybridized to a DNA sequence in the microarray. If the labeled probe contains a cDNA or cRNA whose sequence is  
20 complementary to the DNA at a given spot in the microarray, the labeled probe will hybridize to that spot, where it can be detected by its fluorescence. Since the probes are tagged with fluorescent molecules like Cy3 and Cy5 that emit detectable light

when stimulated by a laser, the probes may be scanned and the emitted light recorded. The probe may be applied to a microarray, DNA, RNA or protein.

In a further embodiment of the invention, a microarray comprises from about 1,000 to about 100,000 DNA sequences. A sample is obtained from the patient's blood cells and is labeled with a first label, and a second RNA sample which serves as a control is labeled with a second label. The first label and the second label have different emission wavelengths. The labels may be fluors, biotinylated markers or other suitable markers. The labeled patient sample and the labeled control samples are mixed and hybridized to the microarray, or they are hybridized to separate arrays. Generally the microarray is then rinsed to remove any non-hybridized samples. The light emitted from the fluors may be measured using any method known in the art, such as commercially available scanners. The relative abundance of the patient and control samples hybridized to the various DNA sequences of the microarray are determined and a pattern is captured.

In yet another embodiment of the invention, the RNA is isolated from the blood of the hypoglycemia, hypoxia, status epilepticus, ischemic stroke, hemorrhagic stroke, and controls. The RNA is purified using standard methods, and then transcribed either into labeled cDNA or into labeled cRNA. These samples are then applied to custom microarrays that are fabricated using the methods for suppressive subtraction hybridization, or custom arrays made from commercially available cDNA libraries. The experimental samples are labeled with Cy3 and the untouched control or sham control samples are labeled with Cy5. The two samples are mixed and applied to a cDNA array produced from all available rat cDNAs, or from an array produced

from cDNAs obtained from the suppressive subtractive hybridization. Alternatively, the samples could be applied to currently available commercial arrays from Incyte, Affymetrix, Research Genetics, and other commercial vendors. Alternatively, samples could be applied to proteomic/ protein microarrays.

5           After a pattern of expression has been captured and defined, an injury database can be established for the injury state. Once an injury database is established for the injury state, only one fluorescent dye is necessary to capture the pattern of expression for subsequent samples as the pattern will be compared to the established injury database.

10           An example of a commercially available microarray is an Affymetrix chip. These arrays are fabricated using spatially patterned, light-directed combinatorial chemical synthesis, and contain hundreds of thousands of oligonucleotides immobilized on the glass surface of the arrays (Affymetrix, Santa Clara, CA). For most sequences or EST there are 16 probe 20mer oligonucleotide pairs, of which 8 a  
15 perfect match and 8 are a mismatch where one nucleotide is changed in the middle of the sequence. Each array also contains a number of reference sequences, which after standards are added allows normalization and quantification of the data. The human U95A array is used, having 13000 sequences and EST's.

          In an embodiment of the invention, the expression levels of the molecules,  
20 captured on the microarray, are ranked from the lowest expressed molecule being assigned a rank of 1 to the most highly expressed molecule. For example, if 100,000 molecules were assessed from a single blood sample, the lowest expressed molecule would be assigned a value of 1 and the most highly expressed molecule a value of

100,000 with every other molecule having a value in between. The ranks of the molecules of individuals with a specific injury or on a specific medication are compared to other individuals with other conditions or to normal healthy controls.

In a further embodiment of the invention, the determination of a pattern of expression further comprises ranking the genes of the captured pattern of expression. The expression levels of the genes, captured on the microarray, are ranked from the lowest expressed gene being assigned a rank of 1 to the most highly expressed gene. For example, if 100,000 genes were assessed from a single blood sample, the lowest expressed gene would be assigned a value of 1 and the most highly expressed gene a value of 100,000 with every other gene having a value in between. The ranks of the genes of individuals with a specific injury or on a specific medication are compared to other individuals with other conditions or to normal healthy controls.

In one embodiment of the invention, microarrays are used to capture the pattern of protein expression. The protein is isolated from either whole blood and/or from white blood cells isolated from whole blood. The protein is then applied to a protein microarray. A protein microarray may be composed of antibodies to all known proteins, antibodies to selected protein subsets, or proteins themselves.

In yet another embodiment of the invention, protein detection is used. Protein detection may include multiple mass spectrophotometric analyses performed in parallel or any other method of detecting hundreds to thousands of proteins at one time from a single blood sample from a single patient. The proteins and antibodies are detected using mass spectrophotometric, fluorescent, radioactive or other techniques and the expression levels of each protein assessed in a manner analogous

to detection of multiple RNA species on current oligonucleotide and cDNA microarrays.

In yet another embodiment of the invention, the determination of a pattern of expression further comprises ranking the proteins of the captured pattern of expression. The expression levels of the proteins, captured on the microarray, are ranked from the lowest expressed protein being assigned a rank of 1 to the most highly expressed protein. For example, if 100,000 proteins were assessed from a single blood sample, the lowest expressed protein would be assigned a value of 1 and the most highly expressed protein a value of 100,000 with every other protein having a value in between. The ranks of the proteins with individuals with a specific injury or on a specific medication are compared to other individuals with other conditions or to normal healthy controls.

Any expression method known in the art may be used to define the pattern of expression captured. A preferred method is the Significance Analysis of Microarrays (SAM) and class prediction, as taught by Tusher, *Proceedings National Academy of Sciences*, 98: 5116 (2001); Golub et al., *Science*, 286: 531-537(1999). Other expression methods are available, including neural network modeling, clustering, computer programs, and entropy methods, and could be used as alternatives.

The significance analysis of microarray (SAM) and class prediction may be used to define the pattern of expression captured. The significance analysis of microarrays uses permutations of repeated measurements to estimate the percentage of genes or proteins identified by chance. Once the molecules are identified that are regulated in a specific injury, this set of molecules is said to define the pattern

expression for that injury. To determine whether an unknown sample is consistent with the normal pattern of expression or is consistent with the pattern for a specific injury, the following general procedure is followed. The expression value for each molecule in the unknown sample is compared to the expression value in the normal set of molecules and in the injury set of genes or proteins. A class prediction method is then used to determine whether the unknown sample fits the normal or injury pattern. To do this, the expression value for each molecule is determined to be closer to the control or the injury state, and a weighted vote is made for each molecule for the injury pattern. The diagnosis of the injury is made if  $PS > 0.3$  when PS is the prediction strength, defined as  $PS = (V_W - V_L) / (V_W + V_L)$ . If there is no difference between the samples, then PS will equal zero and the sample would fall in the class of the control or healthy blood sample. If  $PS > 0.3$ , then the sample would be classified as the injury state.

In one embodiment of the invention, the most regulated genes or proteins for a given condition that had the lowest variance may be identified using SAM analysis for various medical, neurological, genetic and other conditions. These regulated genes or proteins may be used to define a pattern for each condition, a class prediction, that would be used to analyze unknown samples to determine whether they would fit the pattern for a specific disease or condition or not with a 90, 95 or 99% confidence level.

Once the pattern of expression is captured and defined, the pattern of expression exhibited by the obtained blood cells is compared to an injury database to assess the injury. This database may comprise a pattern of expression or multiple

patterns of expression based on a specific organ, a specific injury cause or disease, or combinations thereof. Further, the database may be a commercially available database or a database created from the pattern of expression captured and defined by the obtained blood cells.

5 In one embodiment of the invention, injury databases for hypoxia, status epilepticus and hypoglycemia, are prepared using blood cell samples. These databases are used to assess the injury of an individual based on the comparison between the pattern of expression of the individual and pattern of expression of the database.

10 The embodiments, as set forth above, can be used for any injury as the blood expression will differ with each and every different injury and the database will remain constant.

## **EXAMPLES**

In the examples and throughout the present specification, parts and  
15 percentages are by weight unless otherwise indicated.

### **EXAMPLE 1**

This example demonstrates the use of the claimed invention to assess hypoxia, status epilepticus, hypoglycemia, ischemic stroke, and hemorrhagic stroke in individuals. One day after hypoxia, status epilepticus, hypoglycemia, ischemic  
20 stroke, and hemorrhagic stroke are produced in adult rats, RNA or protein is isolated from the blood cells and from the brains of these animals. Suppressive-subtractive hybridization is performed on the isolated RNA or protein. The clones, obtained from the suppressive-subtractive hybridization, or the isolated RNA or protein are

sequenced. The pattern of genes or proteins expressed in the blood cells following each of these types of injury – hypoxia, status epilepticus, hypoglycemia, ischemic stroke, and hemorrhagic stroke is captured. The pattern of gene or protein expression is defined using an expression method, which then forms a genomic or proteomic organ injury database, which is used in assessing injury in the individuals.

More specifically, adult Sprague Dawley rats (300-350gm males) are housed in a fully AAALAC accredited Animal Research Facility. All animals are examined upon receipt and any animals with symptoms of disease or other problems are sacrificed. Animals are fed ad libitum, with fresh food and water provided several times weekly. Cages are cleaned on a regular schedule.

A custom hypoxia chamber is constructed comprising four identical chambers wherein inlet and outlet air is controlled and monitored. Any oxygen concentration (0-100%, by volume) can be achieved using computer controlled valves and pumps. The inlet and outlet oxygen concentration in each chamber is measured continuously, as is carbon dioxide, temperature and humidity. The oxygen concentrations can be ramped up or down over any period of time (seconds to hours). Generally, the 8%, by volume, oxygen concentration is ramped down over 30 minutes, and the animals remain at 8% oxygen for 6 hours, after which the oxygen is ramped back up to 21%.

Status epilepticus is produced by intraperitoneally injecting a glutamate analogue/excitotoxin, kainic acid (10mg/kg i.p.). Animals with kainate-induced seizures are observed following drug administration to ensure that they continue to have complex seizures over a 30 minute period. Animals with seizures longer than 30

minutes and that have neuronal injury demonstrated histologically are included in the study. Animals injected with kainic acid have diffuse neuronal injury 24 hours later.

Regular insulin (20U sq) is used to induce systemic hypoglycemia. The animals are injected subcutaneously with 10U regular insulin and go into a coma for several hours. The severe hypoglycemia causes severe diffuse neuronal injury. Animals remain hypoglycemic for a period of 4 hours. The hypoglycemia is then reversed with repeated injections of 25% dextrose (25cc) given every half hour for two hours as needed. Prolonged hypoglycemia is required to produce neuronal injury in the brain and other organs. These periods of hypoglycemia induce glucose-regulated protein 75 (GRP75) and other glucose regulated proteins in brain and other organs such as the liver and other tissues.

Ischemic stroke is produced by anesthetizing adult rats with isoflurane. A ventral neck incision is made, and the common carotid artery is isolated. The external carotid artery is ligated, and a 4-0 nylon suture advanced into the external carotid artery and then up the internal carotid artery to the bifurcation of the middle and anterior cerebral arteries. The suture is left in place for two hours to produce an infarction (stroke) in the distribution of the middle cerebral artery. Control animals for the stroke are called “sham” animals. These animals are anesthetized, have the neck incision performed, and arteries isolated, but do not have the suture inserted into the artery and do not have an ischemic stroke.

Hemorrhagic stroke is produced by anesthetizing adult rats with isoflurane. The scalp is incised and a burr hole drilled 0.5mm anterior and 4mm lateral to bregma. A 25 gauge needle was used to deliver 50µl of lysed arterial blood 4mm into

the right striatum. The hemorrhage results in cell death around the margins of the hemorrhage.

Untouched, control animals are not injected or touched prior to the experiment. These animals remain awake, do not undergo surgery, but are housed and  
5 treated like the other animals described above.

All animals are allowed to survive for 24 hours following each treatment. At that time they are deeply anesthetized with ketamine (100mg/kg) and xylazine (20mg/kg) given intraperitoneally. Once anesthetized, the chest is opened and a direct cardiac puncture performed with a syringe and 10cc of blood is aspirated.  
10 Immediately following removal of the blood, the animal is decapitated while deeply anesthetized and the brain removed.

The blood from the animals from the hypoxia group is pooled, as is blood from the animals from the status epilepticus group, the animals from the hemorrhagic stroke group, the animal from the ischemic stroke group, and the animals from the  
15 hypoglycemia group. The blood from the untouched control and the sham-operated control animals is pooled as well. White blood cells are separated on a FICOLL® gradient, and the RNA from each pooled group is extracted with Trizol reagent. Subtractive hybridizations are then performed using commercially available kits (ClonTech) to obtain several separate subtraction libraries: control versus hypoxia  
20 blood; control versus status epilepticus blood; control versus hypoglycemic blood; control versus ischemic stroke blood; and control versus hemorrhagic stroke blood. Generally there are about 500 to about 1000 clones for each subtraction.

Suppressive subtractive hybridization (SSH) is based on a form of PCR that permits exponential amplification of cDNAs that differ in abundance, whereas amplification of RNAs of similar abundance in the control and experimental populations is suppressed. Alternatively, Representational Difference Analysis (RDA) may be used for performing library subtractions.

Poly A<sup>+</sup> RNA from the control bloods (“driver” or “control”) and the hypoxic, hypoglycemic, ischemic stroke, hemorrhagic stroke, or status epilepticus bloods (“tester” or “experimental”) is made, and then quantified on a formaldehyde gel. Each sample is concentrated to a range of from about 1 to about 2 µg/ml. Double stranded (ds) cDNAs are prepared from the two poly A<sup>+</sup> RNA samples by reverse transcription. Second strand cDNA synthesis is then performed and the ds cDNAs are digested with a four-base cutting enzyme (Rsa I) that yields blunt ends. The cut ds cDNAs are digested with a four-base cutting enzyme (Rsa I) that yields blunt ends. The cut ds cDNAs are analyzed on a 1%, by weight, agarose gel.

Following this, the tester ds cDNA pool is divided into two equal portions, and the ds cDNA in one portion is ligated with adaptor 1 and the cDNA in the other portion is ligated with adaptor 2 using T4 DNA ligase. Since the ends of the adaptors do not have a phosphate group, only one strand of each adaptor attaches to the 5' ends of the cDNA. Importantly, the two adaptors (1 and 2R) share a stretch of common sequences that allows them to anneal with each other during PCR. Following successful ligation of the adaptors, hybridization is performed with excess “driver” added to each “tester” sample. The samples are heat denatured and allowed to anneal. The concentration of high and low abundance cDNAs are equalized in the adaptor-

ligated population of cDNAs. The cDNAs are equalized due to second-order hybridization kinetics for these differently expressed cDNAs (ClonTech). There is exponential amplification of rare cDNAs in the “tester” samples. During the second hybridization, the two “tester” samples ligated with adaptor 1 and 2R, and the freshly  
5 denatured “driver” sample are mixed without denaturing. Only the equalized and subtracted single stranded (ss) tester molecules can re-associate and form double stranded hybrids. The ends (site of different adaptors) are then filled in and these new hybrids are amplified by PCR. Molecules missing the primer annealing sites (adaptor 1 and 2R) cannot be amplified due to suppression of PCR.

10 The subtracted library is ligated into the T/A cloning vector (Invitrogen, Inc.) and electroporated into phage-resistant bacterial cells (DH10B), which are then stored in glycerol at -80°C. An aliquot (100µl) of the library is plated on a LB agar plate with the appropriate antibiotic for the purpose of determining the titer of the library. The T/A cloning vector has a B-galactosidase site that provides the mechanism for  
15 color (blue vs white) selection of bacterial colonies that contain a subtracted clone. Positive colonies are inoculated in 96-well plates with antibiotic and 10% glycerol and stored at -80°C. This becomes the original copy of the library. Several controls are performed to help ensure that the procedure worked properly. First, from about 60 to about 80 randomly selected clones are examined on 2% agarose gels to show that  
20 the inserts are of the appropriate sizes ranging from about 0.3 to about 1 kb, and that they are of differing sizes and therefore unique. PCR for G3PDH (glyceraldehyde-3-phosphate dehydrogenase) is performed on the subtracted and unsubtracted libraries

to ensure that the ubiquitously expressed and unregulated G3PDH is not expressed in the subtracted library.

Clones that show a two fold or greater induction by hypoxia, hypoglycemia ischemic stroke, hemorrhagic stroke, or status epilepticus in the five subtracted  
5 libraries are sequenced and compared to currently available rat sequences (GeneBank). The cloned sequences are also subjected to BLAST (basic local alignment search tool, GenBank database) to determine if they match the sequences of known genes. BLAST is a computer program used to search databases to determine if a sequence is similar to that of known or previously cloned genes.

10 Once a sufficient number of clones are sequenced and their identity determined, genes are selected for further study based upon their expression with each type of injury. For example, glucose regulated genes are induced with hypoglycemia and not with hypoxia and status epilepticus. Hypoxia-inducible factor and its hypoxia-inducible target genes are induced with hypoxia and not with hypoglycemia  
15 or status epilepticus. Catecholamine-related genes, like alpha-adrenergic and beta adrenergic-receptors, are induced to a greater extent following status epilepticus as compared to hypoxia or hypoglycemia. Once candidate clones are identified, then the clones are used to perform Northern blots on RNA from bloods of the hypoxic, hypoglycemic, status epilepticus, ischemic stroke, hemorrhagic stroke and control  
20 groups. Alternatively, PCR is performed on each sample and the PCR products sequenced to confirm gene induction for each group. Each clone is then used to produce a spot on a microarray.

Northern blots are performed to confirm the specificity of the clones for each gene and to quantify RNA induction. After isolation of RNA, it is incubated with DNase (5 U/ml; Promega) and RNAsin (200 U/ml; Promega) at 37°C for 30 min. The RNA is ethanol precipitated, dissolved in water and the OD<sub>260/280</sub> determined. Four  
5 micrograms of RNA are electrophoresed in a 1.5% agarose gel containing 1xMOPS and 7% paraformaldehyde and transferred to a nylon membrane (Nytran, Schleicher and Schuell, Keene, NH) for a period of from about 12 to about 18 hours. The RNA is cross-linked to the membrane with UV light at 254 nm (Stratalinker, Stratagene, CA). The membrane is stained with 0.02% methylene blue and the position of the 18S and  
10 28S bands marked on the membrane. It is then pre-hybridized at 42°C for about 1 hour with a mixture of 6X SSC, 0.1% SDS, 10X Denhardt's reagent and 50 µg/ml heat denatured salmon sperm DNA. Clones are labeled using TdT (Gibco BRL) with <sup>32</sup>P-dATP (DuPont-NEN Research Products) and membranes are hybridized at 37°C overnight in 6X SSC, 1% SDS and 1-4 x 10<sup>6</sup> cpm/ml of the labeled probe. After  
15 hybridization, the membranes are washed to a maximum stringency of 6X SSC and 0.1% SDS (sodium dodecyl sulfate) at 55°C. The membranes are then covered with Kodak SB5 autoradiographic film for a period of from about 4 to about 12 hours and developed in Kodak GBX developer. Blots are quantified using an MCID (St. Catherine's, Ontario, Canada) image analysis system.

20 The fabricated microarray is used to capture the pattern of expression in the injury states of hypoxia, status epilepticus, hypoglycemia, ischemic stroke, and hemorrhagic stroke. An expression method defines the pattern of expression and the pattern of expression is compared to an injury database to assess the injury.

## **EXAMPLE 2**

This example demonstrates the use of the claimed invention to assess hypoxia, status epilepticus, hypoglycemia, ischemic stroke, and hemorrhagic stroke. One day after hypoxia, status epilepticus, hypoglycemia, ischemic stroke, and hemorrhagic stroke are produced in adult rats, RNA or protein is isolated from the blood cells and from the brains of the animals described in Example 1. The pattern of genes or proteins expressed in the blood cells following each of these types of injury – hypoxia, status epilepticus, hypoglycemia, ischemic stroke, and hemorrhagic stroke is captured on a commercially available microarray (Affymetrix chip). The pattern of gene or protein expression is defined using an expression method, which then forms a genomic or proteomic organ injury database, which is used in assessing injury.

The data below demonstrates the pattern of gene expression in the blood cells and in the brain following specific pathological insults using genomic profiles based on commercially available microarrays. The data demonstrate how a pattern of gene expression is derived, and that the patterns of gene expression for the different pathological states are different from each other. The tables give lists of genes induced in blood and in the brain of animals exposed to hypoxia, stroke, and status epilepticus as compared with untouched control or sham operated control animals. As shown in Figure 1a and 1b, many genes upregulated or downregulated by each experimental condition were modulated in two or more groups. Figure 2 presents a cluster analysis of the pattern of expression obtained from individuals with kainate, insulin-glucose, hypoxia, brain ischemia, brain hemorrhage, as compared to sham surgery and untouched control individuals.

For the tables of genes induced in the blood, the genome expression of blood in the hypoxic animals (3 animals) was compared to the genome expression of blood in untouched control animals (3 animals). The genome expression of blood in the animals with status epilepticus (3 animals) was compared to the genome expression of blood in the untouched control animals (3 animals). The genome expression of blood in the animals with stroke (3 animals) was compared to the genome expression of blood in the sham operated control animals (3 animals). In each case the accession number of the gene and the fold change in gene expression is given – with a maximum estimate and a minimum estimate.

Tables 1 to 4 set forth lists of genes induced in the blood in the different conditions. Tables 5 and 6 set forth lists of genes induced in the brain in the different conditions. Note that the genes induced in the blood are different from the genes induced in the brain. Therefore, different organs express different genes. In addition, the genes induced by hypoxia in the blood are different from the genes induced by hypoxia in the brain. That is, the same stimulus induces different genes in different organs. Lastly, even though similar genes are induced in the brain by ischemia (stroke) and kainic acid-induced seizures, there are many differences in the gene expression between the two. Therefore, the pattern of gene expression in the brains of ischemic animals is distinctive from the pattern of expression of the kainate animals, and this pattern can be used to diagnose the different conditions of stroke and status epilepticus, even though many of the same genes are induced in the two conditions.

Table 1 sets forth genes induced in the blood of rats 24 hours following 6 hours of 8% hypoxia (n=3 rats) as compared with genes expressed in the blood of

untouched control rats (n=3 rats). The accession number of the gene is given, the name of the gene is given where known, the average fold induction is given, as well as the minimum fold induction is given for each gene. A number of the genes are ESTs that have not yet been subjected to a BLAST search. This list represents the number of genes induced on arrays that contained 8000 genes.

**Table 1:**

<u>Accession No.</u>	<u>Name</u>	<u>Average</u>	<u>Minimum</u>
X62950mRNA f at	pBUS30 with repetitive elements	10	4.8
rc AA891933 at		9	1.9
X06827 at	porphobilinogen deaminase	7.1	4.1
rc AA894273 at		6.1	2.7
X63675 at	Pim-1	6	1.8
D13978 s at	argininosuccinate lyase	5.1	1.9
X62325cds r at	T cell receptor V-alpha J-alpha	5	1.8
rc AA891737 at		5	1.6
rc AA891920 at		4.9	2.7
S65555 g at	gamma-glutamylcysteine synthetase light chain	4.5	2.1
rc AI233261 i at		4.4	1.5
X06827 g at	porphobilinogen deaminase	4.3	2
rc AA800745 at		4.3	1.5
X17053mRNA s at	Rat immediate-early serum-responsive JE gene	4.2	3.9
rc H33723 at		4.1	2.6
S65555 at	gamma-glutamylcysteine synthetase light chain	4.1	1.9
U39875 at	EF-hand Ca2+-binding protein p22	4	1.8
rc AI059042 at		4	1.7
M91234 f at	VL30 element	3.9	2.4
U73030 at	pituitary tumor transforming gene (PTTG)	3.9	1.6
Y13275 at	D6.1A protein	3.9	1.5
M59936cds at	connexin-31	3.8	2.1
rc AA852046 s at		3.8	2.1
rc AA852046 s at		3.8	2.1
rc AI145680 s at		3.8	1.6
rc AI045315 f at		3.8	1.4
M15474cds s at	alpha-tropomyosin gene	3.7	2.4
AF102552 s at	270 kDa ankyrin G isoform	3.7	1.7
M91235 f at	VL30 element	3.6	2.4
U07201 at	asparagine synthetase	3.5	2
AB015194 at	50 kD glycoprotein (Rh50)	3.5	1.8
U25650_f at	low affinity nerve growth factor receptor precursor (LNGFR)	3.5	1.4
X17053cds s at	Rat immediate-early serum-responsive JE gene	3.4	2.1
Y00350 at	uroporphyrinogen decarboxylase	3.4	1.9
rc AA891880 g at		3.4	1.3
rc AI235890 s at		3.3	2.5

Accession No.	Name	Average	Minimum
rc AI235890 s at		3.3	2.3
AB000199 at	cca2	3.3	1.3
M62388 at	ubiquitin conjugating-protein	3.2	1.8
X89225cds s at	L-like neutral amino acid transport activity protein	3.2	1.5
rc AA858607 at		3.2	1.4
X82396 at	cathepsin B	3.1	2.3
X62660mRNA g at	glutathione transferase subunit 8	3.1	1.3
M60666 s at	alpha-tropomyosin 2	3	1.7
rc AA926149 g at		3	1.6
AF076856 s at	small espin	2.9	1.8
rc AA892897 at		2.8	1.7
D90401 g at	dihydrolipoamide succinyltransferase	2.8	1.4
M34134 s at	brain alpha-tropomyosin (TMB-2)	2.8	1.4
rc AA799680 at		2.8	1.4
rc AI029920 s at		2.8	1.3
rc AA891107 at		2.7	1.6
rc AI235585 s at		2.7	1.6
X67948 at	channel integral membrane protein 28	2.7	1.6
AF067790 s at	palmitoyl-protein thioesterase	2.7	1.4
M89945mRNA g at	Rat farnesyl diphosphate synthase gene	2.7	1.4
rc AA819793 at		2.6	1.8
J02592 s at	glutathione S-transferase Y-b subunit	2.6	1.6
rc AA893590 at		2.6	1.6
AF090113 g at	AMPA receptor binding protein	2.6	1.4
M89945mRNA at	Rat farnesyl diphosphate synthase gene	2.5	1.6
rc AI180442 at		2.5	1.5
D63774 at	keratin 14	2.5	1.3
rc AA818025 at		2.4	1.3
rc AI014094 at		2.4	1.3
D86215 at	brain mRNA for NADH-ubiquinone oxidoreductase	2.3	2.1
rc AA874827 at		2.3	1.6
rc AA946368 at		2.3	1.6
U82623 g at	cytacentrin	2.3	1.6
X12554cds s at	heart cytochrome c oxidase subunit VIa	2.3	1.4
AJ009698 g at	embigin protein	2.3	1.3
D10026 s at	glutathione S-transferase	2.2	1.7
rc AA851403 g at		2.2	1.5
U67138 at	PSD-95/SAP90-associated protein-2	2.2	1.4
D38036 at	Truncated TSH receptor	2.2	1.3
rc AA892805 g at		2.2	1.3
rc AI013513 at		2.2	1.3
rc AA851887 s at		2.1	1.6
D13120 s at	ATP synthase subunit d	2.1	1.4
rc AA892888 at		2.1	1.4
U82623 at	cytacentrin	2.1	1.4
D16478 at	mitochondrial long-chain enoyl-CoA hydratase	2.1	1.3
rc AA799612 at		2.1	1.3
AF029240 at	MHC class Ib RT1.S3	2	1.4
J05022 at	peptidylarginine deiminase	2	1.4
rc AI231472 s at		2	1.4
rc AA866477 at		2	1.3

<u>Accession No.</u>	<u>Name</u>	<u>Average</u>	<u>Minimum</u>
rc AA875107 at		2	1.3
rc AI105050 at		2	1.3
rc AA925752 at		2	1.1
AF050663UTR#1_at	norvegicus activity and neurotransmitter-induced early gene	1.9	1.5
X53363cds s at	calreticulin	1.9	1.5
S78154 at	inwardly rectifying ATP-regulated K <sup>+</sup> channel	1.9	1.4
U24489 at	tenascin-X	1.9	1.4
X63722cds s at	vascular cell adhesion molecule-1(VCAM-1)	1.9	1.4
D13212 s at	N-methyl-D-aspartate receptor subunit (NMDAR2C)	1.9	1.3
D78308 g at	calreticulin	1.9	1.3
AF017437 g at	integrin-associated protein form 4 (IAP)	1.8	1.5
X03369 s at	beta-tubulin T beta15	1.8	1.5
D45254 g at	cellular nucleic acid binding protein (CNBP)	1.8	1.4
rc AI146195 at		1.8	1.4
AF020618 at	progression elevated gene 3 protein	1.8	1.3
AF060174 at	synaptic vesicle protein 2C (SV2C)	1.8	1.3
D10587 at	85kDa sialoglycoprotein (LGP85)	1.8	1.3
rc AA799887 s at		1.8	1.3
rc AA859957 at		1.8	1.3
X80395cds s at	rVAT gene	1.8	1.3
rc AA892260 at		1.7	1.4
AF017437 at	integrin-associated protein form 4 (IAP)	1.7	1.3
AF073839 s at	bithoraxoid-like protein	1.7	1.3
Rc AI169631 s at		1.7	1.3
U36444cds#1 at	PCTAIRE-1 protein kinase	1.7	1.3
L38437_at	NADH ubiquinone oxidoreductase subunit (IP13) gene	1.6	1.3
rc AI112237 at		1.6	1.3
rc AA893690 g at		1.5	1.3

Table 2 sets forth genes induced in the blood of rats 24 hours following kainate induced seizures (n=3 rats) as compared with genes expressed in the blood of untouched control rats (n=3 rats). The accession number of the gene is given, the name of the gene is given where known, the average fold induction is given, as well as the minimum fold induction is given for each gene. A number of the genes are ESTs that have not yet been subjected to a BLAST search. This list was shortened to show only those genes induced at least 2.8 fold. Over 100 genes were induced following kainate on arrays that contained over 8000 genes.

**Table 2:**

<u>Accession No.</u>	<u>Name</u>	<u>Average</u>	<u>Minimum</u>
D84485 at	PMSG-induced ovarian mRNA	11.4	3.1
M96159 at	adenylyl cyclase type V	10	2.9
Rc AA955182 g at		9	2.3
AF045464 s at		6.5	2.5
X76697 at	B7 antigen	5.7	2.5
D89863 g at (M-ras)	M-Ras	5.6	2.3
U66566 at	receptor type protein tyrosine phosphatase psi	5.5	4.3
L81138exon	Rps2r gene	5.5	2.3
AF079162 at	patched (ptc)	5.4	3.2
Rc AA894273 at		5.2	2.8
Rc AA799614 at		4.7	2.5
AF102552 s at	ankyrin G isoform	4.6	2.4
M91234 f at	VL30 element	4.4	2.5
L42855 at	RNA polymerase II transcription factor SIII p18 subunit	4.32	3.4
Rc AA852046 s at		4.3	2.5
AF027571 s at	phospholipase C-beta 4 isoform (PLC-b4)	4.15	2.5
Rc AI104924 f at		4.1	3.3
U73030 at		4.1	2.4
Rc AA925529 at		4	3
Rc AA891828 at		4	2.6
M91235 f at	VL30 element	3.9	3
L81136cds f at	Rps2r1 preliminary DNA	3.9	2.7
X06827 at	porphobilinogen deaminase	3.6	3
X60675 at	interleukin 10	3.6	2.3
Z28351exon s at	25-hydroxyvitamin D3 24-hydroxylase	3.5	2.3
AF091563 i at	isolate QIL-LD1 olfactory receptor	3.4	2.4
rc AI102562 at		3	2.4
S54212 at	ciliary neurotrophic factor receptor alpha	2.8	2.6

Table 3 sets forth genes induced in the blood of rats 24 hours following a stroke produced by filament occlusion of the middle cerebral artery (n=3 rats) as compared with genes expressed in the blood of sham operated control rats (n=3 rats). The accession number of the gene is given, the name of the gene is given where known, the average fold induction is given, as well as the minimum fold induction is given for each gene. A number of the genes are ESTs that have not yet been subjected to a BLAST search. This list was produced from arrays that contained over 8000 genes.

**Table 3:**

<u>Accession No.</u>	<u>Name</u>	<u>Average</u>	<u>Minimum</u>
X52196cds at	five-lipoxygenase activating protein (FLAP)	9.5	1.7
rc AA866444 s at		8.8	2.6
Rc AA892851 at		5.6	3.9
rc H31722		5.4	2
L18948 at	intracellular calcium-binding protein (MRP14)	4.1	1.7
rc AA849036		4	2.5
rc AI043796 s at		3.9	2.4
D89093 at	cGMP-binding cGMP-specific phosphodiesterase	3.6	1.8
AF023621 at	sortilin	3.5	2
rc AI639246 at		3.2	1.7
Rc AA957003 at		3.2	1.6
L00603 at	vesicular monoamine transporter	3	2.4
U13396 at	protein-tyrosine kinase (JAK2)	3	2.1
M64986 g at	amphoterin mRNA	3	1.5
L11319 at	five-lipoxygenase activating protein (FLAP)	2.8	1.5
rc AA892851 g at		2.7	2.3
X78605 at	rab4b mRNA for ras-homologous GTPase	2.7	2.3
U49930 g at	ICE-like cysteine protease (Lice)	2.7	1.6
rc AA893534 at		2.6	1.8
D17521 at	protein kinase C-regulated chloride channel	2.6	1.7
U27201 at	tissue inhibitor of metalloproteinase 3 (TIMP-3)	2.6	1.6
M55532 at	carbohydrate binding receptor	2.5	1.8
D13962 g at	neuron glucose transporter (GLUT3)	2.5	1.4
rc AA893664		2.3	1.8
AJ000557cds s at	Janus protein tyrosine kinase 2, JAK2	2.2	1.6
rc AA875206 at		2.2	1.5
D84346 s at	Nap1 protein	2.2	1.4
rc AA800275 at		2.2	1.4
rc AI171962 s at		2.2	1.4
S70011 g at	tricarboxylate carrier	2.1	1.8
AF084186 s at	alpha-fodrin (A2A)	2.1	1.7
L25387 g at	phosphofructokinase C (PFK-C)	2.1	1.6
rc AA892049 at		2.1	1.4
rc AI638939 at		2.1	1.4
U09631 at	VIP2 vasoactive intestinal peptide receptor	2.1	1.4
M93017 at	Rat alternatively spliced mRNA	2.1	1.3
rc AA799402 at		2	1.8
X78949 at	prolyl 4-hydroxylase alpha subunit	2	1.7
rc AA799650 at		2	1.6
rc AA859520 at		2	1.6
U41164 at	Cys2/His2 zinc finger protein (rKr1)	2	1.6
X63995 at	NTT	2	1.6
L01793 at	glycogenin	2	1.3
rc AA891732 at		1.9	1.5
rc AA892511 at		1.9	1.5
rc AI230778 at		1.9	1.5
AF099093 g at	ubiquitin-conjugating enzyme UBC7	1.9	1.4
rc AA893217 at		1.9	1.4

<u>Accession No.</u>	<u>Name</u>	<u>Average</u>	<u>Minimum</u>
rc AA956958 at		1.9	1.4
rc AI045794 at		1.9	1.3
rc AA799637 at		1.8	1.6
rc H31610 at		1.8	1.5
X78606 at	rab28 mRNA for ras-homologous GTPase	1.8	1.5
rc AA875594 s at		1.8	1.4
rc AI171506 g at		1.8	1.4
S70011 at	tricarboxylate carrier	1.8	1.4
rc AA893002 at		1.8	1.3
X61295cds s at	L1 retroposon, ORF2 mRNA	1.8	1.3
rc AA799570 at		1.7	1.5
rc AA874934 at		1.7	1.5
rc AA892642 at		1.7	1.4
X63253cds s at	serotonin transporter	1.7	1.4
rc AA800787 at		1.7	1.3
rc AA891068 f at		1.7	1.3
rc AA892014 r at		1.7	1.3
rc AA892496 at		1.7	1.3
rc AA893237 at		1.7	1.3
rc AI228247 at		1.7	1.3
rc AI639162 at		1.6	1.5
X73371 at	Fc gamma receptor	1.6	1.4
rc AA801286 at		1.4	1.3
U57050 g at	hypertension-related mRNA	1.3	1.3

Table 4 sets forth genes induced in the blood of rats 24 hours following the sham control operation (n=3 rats) as compared with genes expressed in the blood of untouched control rats (n=3 rats). The accession number of the gene is given, the name of the gene is given where known, the average fold induction is given, as well as the minimum fold induction is given for each gene. A number of the genes are ESTs that have not yet been subjected to a BLAST search. This list was produced from arrays that contained over 8000 genes.

**Table 4:**

<u>Accession No.</u>	<u>Name</u>	<u>Average</u>	<u>Minimum</u>
M58040 at	transferrin receptor	5.8	3
D50564 at	mercaptopyruvate sulfurtransferase	5	1.55
U07201 at	asparagine synthetase	4	3
rc AA894273 at		3	1.7
AF087674 at	insulin receptor substrate 2 (IRS-2)	2.9	1.9

<u>Accession No.</u>	<u>Name</u>	<u>Average</u>	<u>Minimum</u>
rc AA858607 at		2.7	1.3
X06827 at	porphobilinogen deaminase	2.6	1.6
D28966 at	prostacyclin receptor	2.6	1.5
rc AA852046 s at		2.6	1.3
E00594cds_at	immunoglobulin E binding factor activity peptide	2.5	1.4
M91235 f at	VL30 element	2.4	1.8
rc AA892897 at		2.3	1.5
M91234 f at	VL30 element	2.2	1.5
rc AA819793 at		2.1	1.7
U12514 at	transcriptional regulator MSX-2 (MSX-2)	2.1	1.4
AF079162 at	patched (ptc)	2.1	1.3
X67948 at	channel integral membrane protein 28	2.1	1.3
X82396 at	cathepsin B	2	1.6
AB015645 at	G protein-coupled receptor	1.9	1.5
L12384 at	ADP-ribosylation factor 5	1.9	1.3
AF087696 at	dlg 2	1.8	1.4
U53486mRNA s at	corticotropin releasing factor receptor	1.8	1.4
rc AA800566 g at		1.8	1.3
X12554cds s at	heart cytochrome c oxidase subunit VIa	1.8	1.3
X63722cds s at	vascular cell adhesion molecule-1	1.4	1.2

The above blood data only catalogues the genes that show an increase of expression in one condition versus the other. Not listed above are an equal number of genes that show down-regulation or decreases following stroke, seizures and hypoxia when compared to controls. The genes that show down regulation are just as important for describing the pattern of gene regulation in blood but are not included the downregulated genes in the above lists for the sake of simplicity. The downregulated genes in the list of hypoxia-regulated genes in brain are set forth below as an example.

The above data show that different genes, for the most part, are induced in the blood cells of rats following stroke, hypoxia and status epilepticus as compared with the controls. In addition, the genes induced in the blood cells of rats following sham control operations differed from the genes expressed in the blood cells of untouched rats. This data suggests that different patterns of expression will occur in the blood

depending on the injury or the cause of the injury. The pattern of expression for each injury is distinct and therefore can be used to assess the injury.

In further support, the following Tables 5 and 6 list those genes induced in the brain following stroke, kainic induced seizures, and hypoxia as compared with 5 untouched controls and sham-operated controls. This data supports the concept that gene expression in the brain differs following different types of injury, just as gene expression in the blood differs following different types of injury.

**Table 5**

Probe Set	Name	Stroke Ischemia (fold change)	Kainic Acid Seizure (fold change)	Hypoxia (fold change)
M86389cds s	Rat hsp 27	361.9	309.2	NC
S82649-r- at	Narp + neuronal activity-regulated pentraxin	251.8	72.5	NC
rc_A1169327_g_	Tissue Inhibitor of Metalloproteinase	239	186.7	NC
z27118cds s	Rat hsp 70	183.4	37.3	NC
aa848563 s a	heat shock protein 70	145	27.1	NC
d00753_at	Rat RNA for contraptin-like protease inhibitor related protein (CPI-26)	134.4	55.4	NC
m14656 at	osteopontin m RNA	79.3	39	NC
x17053RNA_s	rat immediate-early serum response gene	67.2	51.3	NC
jo2722cds at	Rat heme oxygenase gene	68.5	20.2	NC
z75029_s_at	R.norvegicus hsp 70.2 RNA for heat shock protein 70	64.6	12.3	NC
m36317_s_at	Rat thyrotropin-releasing hormone (TRH) precursor	63.5	30.4	NC
rc aa998683	heat shock protein 27	60.6	50.5	NC
ab002588 at	glycerol 3-phosphate dehydrogenase	53.3	52.4	
m23566exon s	alpha-2-macroglobulin gene	53.2	NC	NC
rc ai045030	C/EBP	52	21	NC
x07266 cds s	Rat RNA for gene 33 polypeptide	51.7	21.7	NC
af028784RNA	GFAP	49.7	52.2	NC
af025308_f_a	Rattus norvegicus MHC class 1b antigen (RT1.CI) gene	44.4	no	NC
m61875 s at	CD44	41.8	69.4	NC
x76454 at	ril RNA	39.8	50.3	NC
rc aa818604		37.4	7.2	NC
s71196RNA s	BDNF	35.8	NC	NC
M23643cds s	TRH	35.1	12	NC
x59864RNA_a	Rat ASM15 gene	34	52.2	NC

Probe Set	Name	Stroke Ischemia (fold change)	Kainic Acid Seizure (fold change)	Hypoxia (fold change)
m26744_at	interleukin 6 (IL6) RNA	32.2	NC	NC
L16764_s_at	heat shock rotein 70 (HSP70) RNA	32.2	10.5	NC
L18948_at	intracellular calcium-binding protein (MRP14) RNA	30	NC	NC
rc_h33003_at	EST	28.5	36.7	NC
s66024_g_at	transcriptional repressor CREM	28.3	2.8	NC
s66184_s_at	lysyl oxidase	27.4	5.7	NC
m19651_at	Fra-1	26	11.6	NC
u18982_s_at	Fra-2	25.9	NC	NC
af039583	decay-accelerating factor	24.7	NC	NC
x52498cds_at	TGFB-1	24.4	12.3	NC
J02962_at	Rat IgE binding protein RNA	24.1	27.7	NC
rc_aa893770	EST	24.1	NC	NC
U22414_at	macrophage inflammatory protein- 1alpha RNA	23.8	NC	NC
af075383_at	suppressor of cytokine signaling-3 (SOCS-3) RNA	22.9	17.4	NC
U12187_at	ras-related protein (rad) RNA	22.7	7.7	NC
rc_aa892333	EST	21.9	10.3	NC
rc_aa893244		21.9	12.5	NC
x17053cds_s	Rat immediate-early serum- responsive JE gene			
U18729_at	cytochrome b558 alpha-subunit RNA	21.4	21.9	NC
rc_aa946503	EST	21.3	9	NC
x59864RNA_g	Rat ASM15 gene	21.1	23.7	NC
rc_aa799396	EST	21	2.5	NC
U05014_g_at	PHAS-1 RNA	20.6	17.3	NC
af087943_s_a	CD14	19.8	8.2	NC
M65149_at	Rat CELF RNA	19.7	7.2	NC
L32132_at	Rat lipopolysaccharide binding protein RNA	19.6	7.3	NC
U09540_at	cytochrome P450 (CYP1B1) RNA	19.2	15.3	NC
S76758_i_at	BDNF	18.5	NC	NC
X17163cds_s	c-jun	17.5	10.5	NC
U24441_at	gelatinase B	17.4	22.4	NC
rc_ai639363	rx03855 EST	17.1	NC	NC
rc_aa799773_at	EST	16.9 ?	NC	NC
rc_ai179610	EST	15.9	3.9	NC
af053312_s_a	CC chemokine ST38 precursor	15.7	3.4	NC NC
s77528cds_s	rNFIL-6=C/EBP-related transcription factor	15.7	NC	NC
d88666	PS-PLA1	15.5	9.4	NC
rc_ai169327_at	EST	15.4	8.9	NC
M64795_f_at	Rat MHC class I antigen gene	15.2	no	NC
x73371_at	Fc gamma receptor	14.5	10.7	NC
x71898_at	urinary plasminogen activator	14.5	8.8	NC

Probe Set	Name	Stroke Ischemia (fold change)	Kainic Acid Seizure (fold change)	Hypoxia (fold change)
	receptor 1			
U42719_at	C4 complement protein RNA	14.1	20.7	NC
rc_aa891911	EST	14	8.8	NC
M11597_at	Rat alpha-type calcitonin gene-related peptide RNA	13.7	9.1	NC
L105489_at	Rat heparin-binding EGF-like growth factor RNA	13.1	10.5	NC
X56306_s_at	Rat RNA of delta-preprotachykinin-a splicing variant of substance P	12.9	10.4	NC
rc_aa893280	EST	12.5	9.8	NC
AFO13144_at	MAP-kinase phosphatase (cpg21) RNA	12.3	NC	NC
M24067_at	plasminogen activator inhibitor-1 (PAI-1) RNA	12.2	6.3	NC
z54212_at	epithelial membrane protein-1	12.2	18.9	NC
af004811	moesin RNA	12	23.7	NC
d26393exon_s	Rat HK2 gene for type II hexokinase, exon 1 and promoter region	12	5.8	NC
rc_ai176658	EST	11.9	12.9	NC
M26745cds_s	Rat interleukin 6 (IL6) gene	11.7	NC	NC
x67948_at	channel integral membrane protein 28	11.5	8.9	NC
x03347cds_g	FBR-murine osteosarcoma provirus genome	11.2	NC	NC
x13044_g_at	MHC-associated invariant chain gamma	11.1	9	NC
u31599	MHC class II-like beta chain (RT1.Dmb) RNA	11.1	11.9	NC
rc_aa800587	EST	11	NC	NC
rc_aa859878	EST	10.9	NC	NC
Y00396RNA_a	c-myc	10.8	6.9	NC
D15069_s_at	adrenomedullin precursor	10.8	NC	NC
rc_ai230255	EST	10.7	NC	NC
M31837_at	Rat insulin-like growth factor-binding protein (IGF-BP3)	NC		
m11794cds#2	Rat metallothionein-2 and metallothionein-1 genes	10.6	3.8	NC
M64785_g_at	Rat vasopressin (VP) RNA	10.4		NC
rc_ai102562	EST	10.3	2.9	NC
U06434_at	Rat vasopressin (VP) RNA	10.3	no	NC
z12298cds	dermatan sulfate proteoglycan-II (decorin)	10.2	no	NC
u92081RNA_s	epithelial cell transmembrane protein antigen precursor (RT140) gene	10.2	9.8	NC
re_ai009405	EST	10.2	7.8	NC
D11445exon#1	Rattus norvegicus gene for gro,	10.1	NC	NC



Probe Set	Name	Stroke Ischemia (fold change)	Kainic Acid Seizure (fold change)	Hypoxia (fold change)
rc aa894338	EST	7.6	5.7	NC
rc aa875126	EST	7.6	8	NC
L33869 at	ceruloplasmin RNA	7.6	3.2	NC
rc aa859827		7.6	15.9	NC
AF081503	inhibitor of apoptosis protein (rIAP)	7.5	NC	NC
U15550	tenascin-C RNA	7.2	3.6	NC
U09401-s at	tenascin RNA	7.1	5.5	NC
s67722 s at	cyclooxygenase isoform COX-2	7	2.2	NC
s61865_s at	syndecan=heparan sulfate proteoglycan core protein	7	3.3	NC
rc ai619318	EST	7	NC	NC
rc ai045858	EST	6.9	6.2	NC
d30649RNA s	phosphodiesterase 1	6.9	6.1	NC
L25925 s at	cyclooxygenase-2 RNA	6.7	2.1	NC
U96490 at	Rattus norvegicus liver RNA	6.7	NC	NC
rc aa875131		6.7	NC	NC
Af030091UTR#1	cyclin ania-6a RNA	6.6	NC	NC
j05132_s at	Rat 3-methylcholanthrene-inducible truncated UDP	6.6	9.3	NC
D14869_s at	prostaglandin E2 receptor EP3 subtype (rEP3)	6.5	NC	NC
rc aa891901	EST	6.5	NC	NC
M63101cds at	Rat interleukin 1 receptor antagonist gene	6.3	NC	NC
J05122 at	peripheral-type benzodiazepine receptor	6.3	6	NC
x60769RNA s	silencer factor B	6.3	2.4	NC
x96437RNA g	PRG1 gene	6.2	2.1	NC
x07285cds s	basic fibroblast growth factor	6.2	7.1	NC
x06769cds g	c-fos	6.2	NC	NC
L27060 at	phosphodiesterase RNA	6.1	NC	NC
AJ002940cds	retinoic acid receptor alpha 1	5.9		NC
L32591RNA a	GADD45 RNA	5.9	3.9	NC
D84418 s at	chromosomal protein HMG2	5.9	4.5	NC
rc aa892553	EST	5.8	7.9	NC
k02184 at	Rat major cute phase alpha-1 protein (MAP)	5.8	2.8	NC
rc aa957003	EST	5.8	NC	NC
M8310 g at	SM22 RNA	5.8	NC	NC
L27059 s at	phosphodiesterase RNA	5.7	NC	NC
rc ai639338	EST	5.6	NC	NC
M34134 s at	alpha-tropomyosin (TMBr-2) RNA	5.6	NC	NC
L20681 at	Rat proto-oncogene (Ets-1) RNA	5.5	NC	NC
x0651RNA-s	Rat RNA for syndecan	5.5	4.6	NC
L14610 at	Rat transcription factor RZR-beta gene	5.5	NC	NC
rc A1070295	EST	5.5	3.5	NC
rc ai030286	EST	5.4	NC	NC
x61381cds s	interferon induced RNA	5.4	5.1	NC

Probe Set	Name	Stroke Ischemia (fold change)	Kainic Acid Seizure (fold change)	Hypoxia (fold change)
M55017exon s	Rat nucleolin gene	5.4	6.5	NC
U62667 at	stannicalcin (rSTC) RNA	5.3	NC	NC
rc aa858586	EST	5.3	NC	NC
rc aa8800613	EST	5.3	2.4	NC
u09540 g at	cytochrome P450 (CYP1B1) RNA	5.3	3.6	NC
u69884_at	calcium-activated potassium 0.3 channel rSK3 (SK) RNA	5.3	NC	NC
M98820 at	Rat interleukin 1-beta RNA	5.3	NC	NC
M15644_at	Rat OMP RNA encoding the olfactory neuronal specific protein	5.2	NC	NC
U31599_g_at	MHC class II-like beta chain (RT1. DMb) RNA	5.2	5.6	NC
L13039 s at	annexin II RNA	5.2	2.3	NC
x57523 g at	mtp1RNA	5.2	8.3	NC
rc aa859305		5.2	5.3	NC
d89070cds s	non-inducible carbonyl reductase	5.1	2.3	NC
x63594cds at	RL/IF-1 RNA	5.1	NC	NC
af008650_at	somatostatin receptor-like protein (SLC1) RNA	5.1	3.5	NC
rc aa817854	EST	5.1	5.9	NC
d29766cds#1	Crk-associated substrate, p130	5	5.6	NC
J03624_at	Rat galanin (a neuropeptide) RNA	5	3	NC
rc aa800962	EST	5	NC	NC
rc aa799686	EST	5	6.3	NC
M60616_at	Rat collagenase (UMRCCase) RNA	4.9	NC	NC
rc A1014163	EST	4.9	2.3	NC
x63594cds g	RL/IF-1 RNA	4.8	NC	NC
ab005900_at	endothelial receptor for oxidized low density	4.8	NC	NC
af036537	homocysteine respondent protein HCYP2 RNA	4.7	NC	NC
z22812 at	interleukin-1 receptor type 2	4.7	NC	NC
u04835 at	CREMdeltaC-G gene	4.7	2.1	NC
U16674 at	interleukin-12p40 RNA	4.7	NC	NC
D29769 at	bone morphogenic protein-7	4.7	NC	NC
x54686cds at	pJunB gene	4.6	NC	NC
rc ai639457	EST	4.6	NC	NC
L46593cds at	small proline-rich protein (spr) gene	4.6	4	NC
af28784cds#	glial fibrillary acidic proteins alpha and delta (GFAP) gene	4.6	6.2	NC
m80633 at	Rat adenylyl cyclase type (IV) RNA	4.6	5.2	NC
rc aa799448	EST	4.6	NC	NC
x60351cds s	alpha B-crystallin	4.5	2.4	NC
s82649_s_at	Narp=neuronal activity-regulated pentraxin	4.5	2.2	NC
u78102 at	krox20 RNA	4.5	NC	NC
rc aa926129	EST	4.5	4.9	NC
x98377 at	RNA for emerlin	4.5	NC	NC

Probe Set	Name	Stroke Ischemia (fold change)	Kainic Acid Seizure (fold change)	Hypoxia (fold change)
rc ai639233	EST	4.4	NC	NC
x95986RNA#1	CBR gene	4.4	NC	NC
af087944RNA	monocyte differentiation antigen CD14 gene	4.4	2.6	NC
RC AA891041	EST	4.3	NC	NC
j04563 at	Rat cAMP phosphodiesterase RNA	4.3	5.4	NC
rc ai233219	EST	4.3	NC	NC
u33500 g at	retinol dehydrogenase type II RNA	4.3	NC	NC
rc ai169756	EST	4.3	1.7	NC
rc aa900476	EST	4.2	NC	NC
L32591RNA_g	GADD45 RNA	4.2	3	NC
rc aa875126	EST	4.2	8.7	NC
L20913_s_at	vascular endothelial growth factor form 3 RNA	4.2	NC	NC
x71127 g at	complement protein C1q beta chain	4.1	3.6	NC
af083269 at	p41-Arc RNA	4.1	3.3	NC
rc aa799773	EST	4.1	4.7	NC
rc ai639402	EST	4.1	NC	NC
a30543cds_s_	p-Meta-a RNA for CD44 surface protein from patent WO9117248	4.1	4.4	NC
aj222813_s_a	precursor interleukin 18 (IL-18)	4.1	3.8	NC
rc ai6139302	EST	4	NC	NC
rc ai639161	EST	4	7.5	NC
rc aa946044	EST	3.9	2.8	NC
m19257_at	Rat cytosolic retinol-binding protein (CRBP) RNA	3.9	4	NC
Y10619cds at	transcriptional regulator, Relax	3.8	3.5	NC
x99121RNA#1	RT6 gene, exon 2, testis	3.8	NC	NC
x74565cds_g_	TBFII RNA for polypyrimidine tract binding	3.8	5.4	NC
d17370 g at	cystathionine gamma-lyase	3.8	3.8	NC
af086624_s_a	serine threonine kinase (pim-3) RNA	3.8	NC	NC
m13979_at	Rat brain and all other organ glucose-transporter protein RNA	3.8	2.1	NC
U13396 at	protein-tyrosine kinase (JAK2) RNA	3.7	NC	NC
d00913 g at	intercellular adhesion molecule-1	3.7	NC	NC
rc aa799323	EST	3.7	NC	NC
d90404 at	cathepsin C	3.7	2.8	NC
d89069 f at	inducible carbonyl reductase	3.7	NC	NC
af053362_at	Rattus norvegicus death effector domain-containing protein DEFT RNA	3.7	NC	NC
m60753_s_at	catechol-O-methyltransferase RNA	3.7	4.5	NC
rc aa891576	EST	3.6	NC	NC
m18330_at	Rat protein kinase C delta subspecies	3.6	3.3	NC
m32062 at	Rat Fc-gamma receptor RNA	3.6	1.5	NC
rc aa866443	EST	3.6	NC	NC



Probe Set	Name	Stroke Ischemia (fold change)	Kainic Acid Seizure (fold change)	Hypoxia (fold change)
	protein 4 (ania-4) RNA			
rc aa800701	EST	3.2	NC	NC
rc aa945737	EST	3.2	NC	NC
rc ai070295	EST	3.2	1.9	NC
M90661_at	Rattus norvegicus insulin receptor-related receptor-alpha subunit RNA	3.2	NC	NC
U49930_g_at	ICE-like cysteine protease (Lice) RNA	3.2	2.7	NC
M92433exon#1	Rattus norvegicus nerve growth factor-induced clone C (NGFI-C) gene	3.1	NC	NC
rc ai639149	EST	3.1	NC	NC
rc aa859740	EST	3.1	NC	NC
D10729_s_at	Rat RNA for proteasome subunit RC1	3.1	4.9	NC
x91810_at	R.norvegicus RNA for Stat3 protein	3.1	NC	NC
x62952	R.norvegicus RNA for vimentin	3.1	3.2	
rc ai178267	EST	3.1	NC	NC
af020618_gc_a	Rattus norvegicus progression elevated gene 3 protein RNA			
d00575_at	Rattus norvegicus RNA for pituitary glycoprotein hormone alpha-subunit precursor, complete cds	3.1	NC	NC
rc aa892578	EST	3.1	2.7	no

NC= No Change. In the above table there were no changes of the above genes with hypoxia.

5 Table 6

Probe Set	Name	Induction	Fold Change
rc AA799861_g_at	interferon regulatory factor 7	I	32.9
U42719_at	C4 complement protein	I	20.8
M64791_at	salivary proline-rich protein (RP4)gene	I	7.2
rc AA799861_at	interferon regulatory factor 7	I	7.1
rc A1045858_at	FK506 binding protein 1a	I	6.7
rc AA946503_at	alpha 2 mu globulin-related protein	I	5.7
rc AI172247_at	xanthine dehydrogenase	I	5.7
rc_AA926129_at	Sacm21/RT1-A intergenic region, partial RT1-A gene for MHC class I ant	I	5
U80915_s_at	EAAT4 Na+-dependent glutamate transporter	I	4.9
rc_AA893822_at	C3H DNA damage repair and recombination protein RAD52	I	4.7
rc AA639161_at	asparaginyl-tRNA synthetase	I	4.5

Probe Set	Name	Induction	Fold Change
M83107 g at	SM22 RNA	I	4.5
x07285cds s at	basic fibroblast growth factor	I	4
x97754	17-beta-hydroxysteroid dehydrogenase type 1	I	3.9
rc_AI638951_at	DCoH gene; pterin-4a-carbinolamin dehydratase	I	3.6
rc_AI639173_at	Homo sapiens genomic DNA, chromosome 8p11.2	I	3
rc_AI639088_at	Mus musculus clone UWGC: mbac82 from 14D1-D2	I	2.9
rc_AI639528_at	KIAA0772 gene product	I	2.9
rc_AA894226 g at	Cpn 10-rs5 pseudogene	I	2.8
x61381cds s at	interferon induced RNA	I	2.8
x13905cds at	ras- related rab1B protein	I	2.8
rc_AA946044 s at	Lyn B tyrosine kinase	I	2.7
M62889 s at	sucrase-isomaltase	I	2.5
M95780 at	G protein gamma-5 subunit RNA	I	2.5
rc_AI177256_at	Human DNA sequence from clone GS1-aa5M3 on chromosome Xq171-2	I	2.5
x06801cds I at	vascular smooth muscle alpha-actin	I	2.4
rc_AA892564 at	6-pyruvoyl-tetrahydroprotein synthase	I	2.4
Y07704 g at	Best5 protein	I	2.4
U83119 f at	retrotransposon ORF2 RNA	I	2.4
rc_AA894016_at	Human DNA sequence from clone RP11-353c18 on chromosome 20	I	2.3
rc_AA892895 I at	ribosomal protein S15	I	2.3
rc_Aa893242 g at	long-chain acyl-CoA synthetase	I	2.3
rc_AI639410_I at	Pneumocystis carinii f. sp. carinii Cdc2 cyclin-dependent kinase	I	2.2
x53581cds#5_f at	long interspersed repetitive DNA containing 7 ORF's	I	2.2
rc_AI639447 at	TANK binding kinase TBK1	I	2.1
rc_AA859740_at	heparan sulfate 6-O-sulfotransferase 1 (Hs6St1). RNA	I	2.1
M58040_at	Rat transferring receptor RNA	I	2.1
rc_AI639410_s at	Pneumocystis carinii f. sp. carinii Cdc2 cyclin-dependent kinase	I	2
M13101cds_f at	Rat long interspersed repetitive DNA sequence LINE4 (L1Rn)	I	2
x07686cds s at	Rat L1Rn B6 repetitive DNA element	I	2
rc_AI012030_at	Rattus norvegicus Matrix Gla protein (Mgp), RNA	I	1.9
rc_AI012534 at	Rattus norvegicus TFIIA small subunit RNA	I	1.9
rc_AA893871_at	Homo sapiens 12p12 BAC RPC111-1018J8	I	1.9
x05472cds#3_f at	Rat 2.4 kb repeat DNA right terminal region	I	1.9
M13100cds#6_f at	Rat long interspersed repetitive DNA sequence LINE3 (L1Rn)	I	1.9

Probe Set	Name	Induction	Fold Change
AF028784cds#1_s_at	Rattus norvegicus glial fibrillary acidic proteins alpha and delta (GFAP) gene	I	1.8
L06040_s_at	Rattus norvegicus 12-lipoxygenase RNA	MI	7.7
M649_f_at	Rattus norvegicus 12-lipoxygenase RNA	MI	7.2
rc_AA891717_g_at	transcription factor; USF 1 gene; USF1 protein	MI	6.9
rc_aa858586_at	chromatin structural protein homolog Supt5hp (Supt5h)	MI	6.4
D10729_s_at	Rat RNA for proteasome subunit RC1	MI	6.3
z46614cds_at	R.norvegicus RNA for caveolin	MI	5.7
rc_AI639498_I_at	Drosophila melanogaster genomic scaffold	MI	5.4
rc_AA859966	inositol 1,4,5-triphosphate receptor type I RNA	MI	5.2
rc_AA893781	Homo sapiens KIAA0050 gene product	MI	4
rc_AA892553	Rattus norvegicus signal transducer and activator of transcription 1 (Stat1) RNA	MI	4
rc_AI639512	surfactant protein A (SP-A)	MI	4
L23077_at	zinc finger protein	MI	3.8
rc_AI639170	Homo sapiens RNA helicase-related protein RNA	MI	3
L00382cds_at	Rat skeletal muscle beta-tropomyosin and fibroblast tropomyosin 1 gene	MI	2.9
rc_AI639339_at	Arabidopsis thaliana chromosome 1 BAC F5D21 genomic sequence	MI	2.8
rc_AA891944	interferon-g induced GTPase	MI	2.7
rc_AI639372	Homo sapiens KIAA0854 protein (KIAA05854)	MI	2.7
x16262_s_at	Rat RNA for alternatively spliced smooth muscle myosin heavy chain	MI	2.6
AF102853	Rattus norvegicus membrane-associated guanylate kinase-interacting protein 1 Maguin-1 RNA	MI	2.5
AJ224680	Rattus norvegicus RNA for glutamic-acid rich protein	MI	2.4
J05132_s_at	Rat 3-methylcholanthrene-inducible truncated UDP-	MI	2.3
rc_AI639342_at	Homo sapiens PAC clone RP4-687K1	MI	2
x52711	Rat RNA for Mx1 protein	MI	2
E12286cds_at	cDNA encoding rat GM2 activator protein	MI	2
rc_AA875646	Homo sapiens clone 25076 RNA sequence	D	13.7
M93257_s_at	Rattus norvegicus catechol-O-methyltransferase RNA	D	13
U50412_at	phosphoinositide 3-dinase regulatory subunit p85alpha RNA	D	10.7
AI007530_f_at	Homo sapiens NADH:ubiquinone oxidoreductase MLRQ subunit	D	10.6
rc_AA924925_at	Dri 42 gene; ER-transmembrane protein	D	9.2
L81138exon_I_at	Rps2r gene	D	6.1

Probe Set	Name	Induction	Fold Change
D64045_s_at	phosphatidylinositol 3-kinase p85 alpha subunit	D	5.2
Y08139_at	dermo-1 protein; helix-loop-helix protein (vascular smooth muscle)	D	5.2
rc_AA818122_f_at	hydroxysteroid sulfotransferase subunit	D	5
rc_AA818593	phosphatidate phosphohydrolase type 2 RNA	D	4.7
rc_AA799480_at	R. norvegicus RNA (pJG116) with repetitive elements	D	4.2
AF050661UTR#1_at	activity and neurotransmitter-induced early gene 9 (ania-9) RNA	D	3.9
rc_AI178971_at	GLUTAMINE SYNTHETASE	D	3.8
L26292_g_at	FSH-regulated protein RNA	D	3.7
S62933_I_at	receptor tyrosine kinase (TrkC(ki14)) RNA	D	3.5
X00975_g_at	Rat MLC2 gene for muscle myosin light chain 2	D	3.4
D82071_at	hematopoietic prostaglandin D synthase	D	3.2
X64563cds_at	plasminogen activator inhibitor 2 type A (PAI2A)	D	3.1
U78102_at	krox20 RNA	D	2.8
rc_H31411_at	Mus musculus chromosome 18 clone	D	2.7
U19866	growth factor (Arc) RNA	D	2.6
M84149_at	Rat IgH chain VJ region RNA	D	2.5
AF075382_at	suppressor of cytokine signaling-2 (SOCS-2) RNA	D	2.4
U17254	immediate early gene transcription factor NGFI-B RNA	D	2.2
U17254_g_at	immediate early gene transcription factor NGFI-B RNA	D	2.2
X60660RNA_g_at	Novel genes for potential ligand-binding proteins in subregions of 3CH134/CL100	D	2.1
S81478_s_at	PTPase=oxidative stress- inducible protein tyrosine phosphatase	D	2
S77492_I_at	bone morphogenetic protein 3	D	1.9
X06769cds_at	C-fos	MD	8.4
D63860_s_at	prepro bone morphogenetic protein-3	MD	3.8
rc_AA859552	skeletal muscle elongation factor-2 kinase	MD	3.4
D26307cds_at	Rattus norvegicus jun-D gene	MD	2.8
rc_AA891041_at		MD	2.3
S74351_s_at	protein tyrosine phosphatase	MD	2.1

This list of hypoxia-regulated genes includes those that increased (I), had a marginal increase (MI) as judged statistically, a decrease (D), or a marginal decrease (MD) as judged statistically. It should be emphasized that the pattern of expression in the blood, brain, and all other organ samples include increased as well as decreased genes or proteins in the injury banks that are formed.

### **EXAMPLE 3**

This example demonstrates the ability to differentiate between male and female blood samples based on patterns of expression. Blood from over 30 patients is collected from healthy controls as well as from patients with various neurological problems, including headaches, seizures, idiopathic Parkinson's disease, progressive supranuclear palsy, and psychosis. The blood cells are isolated, the RNA extracted, and then processed on commercially available chips (human Affymetrix chips). The RNA is analyzed using the statistical program called SAM (Significance Analysis of Microarrays) to determine the genes expressed more significantly in males as compared to females. As shown in Figure 3a and 3b, over 20 genes are highly expressed in the blood samples of males as compared to females. The ticks on the X-axis represent individual patients, the first 11 being females and the next 21 representing males. The Y axis shows the expression of a single gene, Dead Box Y Isoform gene and Ribosomal Protein S4 Y Isoform, respectively. This graph shows that these genes are highly expressed in the blood cells of male patients and are expressed at very low levels in the blood of females.

Tables 7a and 7b below demonstrates the pattern of expression, of the upregulated genes, for males and females respectively. This data demonstrates how the pattern of expression in the blood of individuals is unique and can be used to predict the sex of an individual.

**Table 7a: Upregulated genes in females**

Genbank	Description
X56199	Human XIST, coding sequence a mRNA (locus DXS399E)
U76388	Human steroidogenic factor 1 mRNA, complete cds
D10040	Homo sapiens mRNA for long-chain acyl-CoA synthetase, complete cds
X78710	H.sapiens MTF-1 mRNA for metal-regulatory transcription factor

U09564	U09564 /FEATURE= /DEFINITION=HSU09564 Human serine kinase mRNA, complete cds
U12569	Human mu opioid receptor variant (MOR1) mRNA, complete cds
AF017257	Homo sapiens chromosome 21 derived BAC containing erythroblastosis virus oncogene homolog 2 protein (ets-2) gene, complete cds
M20681	Human glucose transporter-like protein-III (GLUT3), complete cds
AA135683	zl10c08.r1 Homo sapiens cDNA, 5 end
AB002315	Human mRNA for KIAA0317 gene, complete cds
U09877	Human helicase-like protein (HLP) mRNA, complete cds
U45976	Human clathrin assembly protein lymphoid myeloid leukemia (CALM) mRNA, complete cds
AL031775	dJ30M3.3 (novel protein similar to C. elegans Y63D3A.4)
AA705628	zf40a01.s1 Homo sapiens cDNA, 3 end
W26226	22e3 Homo sapiens cDNA
U70451	Human myleoid differentiation primary response protein MyD88 mRNA, complete cds
U27467	U27467 /FEATURE= /DEFINITION=HSU27467 Human Bcl-2 related (Bfl-1) mRNA, complete cds
Y10745	H.sapiens mRNA for inwardly rectifying potassium channel Kir4.2
M83667	M83667 /FEATURE=mRNA /DEFINITION=HUMNFIL6BA Human NF-IL6-beta protein mRNA, complete cds
S82470	S82470 /FEATURE= /DEFINITION=S82470 BB1=malignant cell expression-enhanced gene/tumor progression-enhanced gene [human, UM-UC-9 bladder carcinoma cell line, mRNA, 1897 nt]
AI341565	qq94g11.x1 Homo sapiens cDNA, 3 end
M79321	M79321 /FEATURE= /DEFINITION=HUMLYNTK Human Lyn B protein mRNA, complete cds
M31932	Human IgG low affinity Fc fragment receptor (FcRIIa) mRNA, complete cds
U31383	Human G protein gamma-10 subunit mRNA, complete cds
AB011094	Homo sapiens mRNA for KIAA0522 protein, partial cds
X95735	Homo sapiens mRNA for zyxin
X52015	H.sapiens mRNA for interleukin-1 receptor antagonist
D82351	Human retropseudogene MSSP-1 DNA, complete cds
W28743	51a9 Homo sapiens cDNA
U43774	Human Fc alpha receptor, splice variant FcalphaR a.2 (CD89) mRNA, complete cds
U00115	Human zinc-finger protein (bcl-6) mRNA, complete cds
H15814	yl28b07.s1 Homo sapiens cDNA, 3 end
AL049923	Homo sapiens mRNA; cDNA DKFZp547E2210 (from clone DKFZp547E2210)
AB002344	Human mRNA for KIAA0346 gene, partial cds
U02020	Human pre-B cell enhancing factor (PBEF) mRNA, complete cds
D89974	Homo sapiens mRNA for glycosylphosphatidyl inositol-anchored protein GPI-80, complete cds
AI984234	wz57e04.x1 Homo sapiens cDNA, 3 end
X77094	H.sapiens mRNA for p40phox
J05272	Human IMP dehydrogenase type 1 mRNA complete cds
L18960	Human protein synthesis factor (eIF-4C) mRNA, complete cds
AL008637	Human DNA sequence from clone 833B7 on chromosome 22q12.3-13.2 Contains genes for NCF4 (P40PHOX) protein,cytokine receptor common beta chain precursor CSF2RB (partial), ESTs, CA repeat, STS, GSS
X59739	Human ZFX mRNA for put. transcription activator, isoform 2

U32315	Human syntaxin 3 mRNA, complete cds
L78833	L78833 /FEATURE=cds#4 /DEFINITION=HUMBRCA1 Human BRCA1, Rho7 and vat1 genes, complete cds, and ipf35 gene, partial cds
AB011406	Homo sapiens mRNA for alkaline phosphatase, complete cds
D14874	Homo sapiens mRNA for adrenomedullin precursor, complete cds
AB018306	Homo sapiens mRNA for KIAA0763 protein, complete cds
U24152	U24152 /FEATURE= /DEFINITION=HSU24152 Human p21-activated protein kinase (Pak1) gene, complete cds
U19775	U19775 /FEATURE=cds /DEFINITION=HSU19775 Human MAP kinase Mxi2 (MXI2) mRNA, complete cds
H04668	yj49e08.r1 Homo sapiens cDNA, 5 end
AB007448	Homo sapiens mRNA for OCTN1, complete cds
AL008637	Human DNA sequence from clone 833B7 on chromosome 22q12.3-13.2 Contains genes for NCF4 (P40PHOX) protein, cytokine receptor common beta chain precursor CSF2RB (partial), ESTs, CA repeat, STS, GSS
M81637	Human grancalcin mRNA, complete cds
L36069	Human high conductance inward rectifier potassium channel alpha subunit mRNA, complete cds
L42243	L42243 /FEATURE=cds#3 /DEFINITION=HUMIFNAM08 Homo sapiens (clone 51H8) alternatively spliced interferon receptor (IFNAR2) gene, exon 9 and complete cds s
J05008	J05008 /FEATURE=expanded_cds /DEFINITION=HUMEDN1B Homo sapiens endothelin-1 (EDN1) gene, complete cds
D38583	Human mRNA for calcizzarin, complete cds
AF039656	Homo sapiens neuronal tissue-enriched acidic protein (NAP-22) mRNA, complete cds
J05070	Human type IV collagenase mRNA, complete cds
AF030339	Homo sapiens receptor for viral semaphorin protein (VESPR) mRNA, complete cds
L18960	L18960 /FEATURE= /DEFINITION=HUMEIF4C Human protein synthesis factor (eIF-4C) mRNA, complete cds
AI885381	wl93b01.x1 Homo sapiens cDNA, 3 end

**Table 7b: Upregulated genes in males**

Genbank	Description
M58459	Human ribosomal protein (RPS4Y) isoform mRNA, complete cds
AF000984	Homo sapiens dead box, Y isoform (DBY) mRNA, alternative transcript 2, complete cds
AF000986	Homo sapiens Drosophila fat facets related Y protein (DFFRY) mRNA, complete cds
Y15801	Homo sapiens mRNA for PRKY protein
U52191	Human SMCY (H-Y) mRNA, complete cds
D86324	Homo sapiens mRNA for CMP-N-acetylneuraminic acid hydroxylase, complete cds
AF000994	Homo sapiens ubiquitous TPR motif, Y isoform (UTY) mRNA, alternative transcript 3, complete cds
Z98744	histone H3.1
AF000987	Homo sapiens eIF-1A, Y isoform (EIF1AY) mRNA, complete cds
M30607	Human zinc finger protein Y-linked (ZFY) mRNA, complete cds
AF055581	Homo sapiens adaptor protein Lnk mRNA, complete cds
M60052	Human histidine-rich calcium binding protein (HRC) mRNA, complete cds

#### **EXAMPLE 4**

This example demonstrates the ability to assess Parkinson's disease based a sample's pattern of expression. To study the gene expression in Parkinson's patients, blood from over 30 patients is collected from healthy controls as well as from patients  
5 with a variety of disorders, including idiopathic Parkinson's patients with bradykinesia, rigidity and the characteristic tremor without dementia or evidence of any other neurological findings; progressive supranuclear palsy, bipolar disorder, schizophrenia, epilepsy, and Tourettes. A commercially available kit (Qiagen) is used to the blood cells from the whole blood samples, and total RNA isolated from the  
10 white blood cells. Two thirds of the RNA is used on DNA microarrays, and one third is used for PCR confirmation of the genes that are changed. After the purity of the RNA is checked ( $OD\ 280/OD\ 260=2$ ), cDNA is synthesized from the total RNA and used to make biotin labeled cRNA. The cRNA is then applied to Affymetrix chips, human U95A chips that can screen for the expression of over 13,000 human genes  
15 including 11,000 known genes and 2,000 ESTs, and processed and scanned according to manufacturer's instructions. The chips are scanned twice for each patient sample. Genes that are expressed over two-fold compared to normals are plotted on figures. These genes are confirmed using standard techniques including PCR, Northern blotting or Western blotting. A separate statistical analysis is also applied to the data.  
20 The RNA is analyzed using the statistical program called SAM (Significance Analysis of Microarrays) to define the genes expressed more significantly in Parkinson's patients as compared to other patients. Once this analysis is performed, the data is used to perform a class prediction analysis. As shown in Figure 4, genes SEQ ID

NO:1 and SEQ ID NO:2 are expressed more highly in Parkinson's patients compared to other patients. The expression value of the genes is shown on the Y axis and the individual patients are plotted on the X-axis. The data demonstrates that the pattern of expression may be used to assess Parkinson's injury in an individual.

## 5 **EXAMPLE 5**

This example demonstrates the ability to assess stroke as compared to hemorrhage based on the pattern of expression for each injury. One 20ml venous blood sample (in EDTA, two lavender top tubes) is obtained from patients at 24 hours ( $\pm$  4 hours) following : a large vessel ischemic stroke with a NIHSS of  $\geq$  10;

10 following an intracerebral hemorrhage (ICH) with a NIHSS of  $\geq$  10; or following admission to the University of Cincinnati hospital for other neurological or medical reasons (controls). The blood cells are separated, followed by isolation of total RNA. Ischemic strokes and intracerebral hemorrhages are confirmed by clinical history, clinical neurological examinations, and CT or MRI scans performed within 72 hours.

15 The total RNA is used to synthesize cDNA and then biotin labeled cRNA. This is applied to human Affymetrix chips that are processed and scanned according to the manufacturer's instruction. Affymetrix Gene Chip software is used to determine which genes are scored as being present and absent and which genes show a two fold change following ischemic stroke compared to the controls and compared  
20 to the patients with intracerebral hemorrhages. The data is imported into Gene Spring, a commercially available biostatistic package, that allows for the calculation of fold changes of genes across all of the patients in all three groups, and for cluster analysis as shown in Example 1.

The primary analysis is Significance Analysis of Microarrays, which allows delineation all of the genes that are significantly expressed in ischemic stroke that are different from the genes expressed in the control group and in the intracerebral hemorrhage group, using a false discovery rate threshold of 5% or 10%. This defines  
5 a set of genes that are most reliably expressed following ischemia compared to the other samples. This set of genes is then used to define a prediction set of genes, S. The prediction set S of genes is then used to perform weighted voting on patient samples to determine if a patient sample conforms to the prediction set S or not. The first analysis is done to determine if the set S correctly predicts the initial set of  
10 ischemic samples used to derive the prediction set S. The second analysis determines if the set S correctly predicts a separate, new group of ischemic patient samples.

#### **EXAMPLE 6**

This example demonstrates assessment perfusion state and/or excellent reperfusion, moderate reperfusion and/or poor reperfusion based on patterns of  
15 expression. All patients entered into the tPA/eptifibatide trial in Example 4 receive one of several tPA doses by 3 hours after an ischemic stroke. They also have a CT within the first 3 hours. At 24 hours following the stroke 20cc of anticoagulated (EDTA) blood (two lavender tops) is obtained from patients with a NIHSS of  $\geq 10$ , just as was done in Example 4. The blood cells are isolated, total RNA is purified,  
20 and then processed on human Affymetrix chips as described in Example 4. Using statistical methods defined in Example 4, patterns of expression characteristic of reperfusion as determined by MRA at 24 hours is determined. Also, patterns of expression that differentiates tPA treated patients without intracerebral hemorrhages,

compared to those with tPA associated intracerebral hemorrhages, are determined. Lastly, a specific pattern of expression of patients with ischemic stroke treated with tPA as compared to patients with ischemic stroke not treated with tPA from Example 4 is determined.

5 All patients that receive tPA have a CT brain scan within 3 hours of the stroke, and have a MRI brain study one day later. The MRI evaluation includes a MRA (magnetic resonance angiogram), a diffusion MRI, and one MRI sequence to assess stroke volume (either a flash, T2, gradient echo or other sequence which will be standardized for all patients). MRA studies are evaluated by two independent  
10 neuroradiologists who rate the MRA at 24 hours as showing excellent, moderate or poor reperfusion. In addition, the MRA is evaluated using an MCID computer analysis system (SWANSON). An optical density threshold is set so that the vessels in the non-ischemic hemisphere are detected in the middle cerebral artery distribution which is defined using the same mask in every patient. The area occupied by these  
15 vessels is then computed automatically. Using a mirror image of the same region of the middle cerebral artery distribution in the ischemic hemisphere, the area occupied by the vessels is again computed automatically. Excellent reperfusion will be defined as the value in the ischemic hemisphere being  $> 85\%$  of the non-ischemic hemisphere. Poor reperfusion is defined as the value in the ischemic hemisphere being  $<45\%$  of  
20 the non-ischemic hemisphere. Moderate reperfusion is defined as  $>45\%$  and  $<85\%$ . At least two MRA slices per patient are examined. Hence, there is a qualitative comparison of reperfusion performed, as well as a semi-quantitative comparison of reperfusion as determined by MRA. The pattern of expression of three groups of

patients, excellent, moderate and poor reperfusion are then compared against each other to assess excellent reperfusion, moderate reperfusion or poor reperfusion. These patterns of expression may be used to assess reperfusion state and/or excellent, moderate and/or poor reperfusion of stroke in an individual.

5 **EXAMPLE 7**

The whole blood genomic responses of patients with status epilepticus, single seizures, or syncope are compared between the three conditions.

Adult males (n=10) and females (n=10) (all races between the ages of 18 and 75 years) with status epilepticus are entered into the example. Patients are considered  
10 if they (1) are diagnosed clinically as having had generalized status epilepticus and/or (2) have evidence of status epilepticus by EEG criteria. Clinical evidence of status epilepticus includes either continuous generalized seizures for 30 minutes, or intermittent generalized seizures for 30 minutes during which the patient does not fully recover consciousness. Within 18 to 28 hours of the start of the episode of status  
15 epilepticus, a single venous 12ml blood sample (sterile in EDTA) is obtained. A follow up, second 12ml blood sample is obtained either at discharge when the patient has fully recovered (at least 3 days following the event) or not later than 7 days following the episode of status epilepticus. Data is obtained from the patient's chart on medications received and the temporal relationship of medication doses, the  
20 beginning and end of the episode of status, and the time of the blood sample. Details of the episode of status, including duration of status observed, approximate duration unwitnessed (if any), clinical manifestations (convulsive or subtle), EEG findings, time of any prior episodes of status, the presence of any documented hypoxia or

global ischemia, and the patient's past medical history are also obtained. The time between the end of the status epilepticus and the full recovery of normal cognitive function is documented based upon mini-mental status scores performed every 8 hours by the examining physicians. Outcome at hospital discharge will be recorded.

- 5           Adult males (n=10) and females (n=10) (all races > 18 years old, <75 years old) with single generalized tonic clonic seizures are entered into this example. Patients are considered for this example if they have a history of generalized tonic clonic seizures and sample (sterile in EDTA) is obtained. A follow-up, second 12ml blood sample is obtained within 18 to 28 hours after the patient has single generalized
- 10   tonic clonic seizure. The duration, precise time of the seizure, and timing of any other seizures and their type is obtained from the patient's chart. Other information gathered will include current medication dosages and blood levels, recent changes in medications, and underlying etiology of seizures.

- Approximately 30% of the patients who are admitted to inpatient epilepsy
- 15   monitoring units to evaluate medically refractory seizures have events that are ultimately diagnosed as non-epileptic. These patients serve as non-epileptic controls (n=10) because they have received antiepileptic drugs prior to hospitalization and will have had those drugs tapered or discontinued during the hospitalization like the epileptic subjects. These patient have 12ml blood samples (sterile in EDTA) obtained
- 20   within 18-24 hours of admission, and have a second blood sample obtained 18-24 hours after the witnessed event that is documented by EEG criteria to have been a "non-epileptic" generalized "pseudo-seizure".

Adult males and females (all races > 18 years old, <75 years old) with syncope are entered into this example. Patients who are being evaluated for syncopal episodes by tilt table studies are considered. Each patient has a single venous 12ml blood sample obtained. A follow-up, second 12ml blood sample is obtained within 18-24 hours after the patient has a syncopal episode on the tilt table or as an outpatient. The duration, precise time of the syncope, and timing of any other syncopal episodes and their type and duration are obtained. Other information gathered includes current medication dosages and blood levels, recent changes in medications, and the etiology of syncope if known. Any evidence for recent severe global ischemic or anoxic events is evaluated.

RT-PCR is performed on the blood samples of all patients with status epilepticus (within 24h of the event and then 3-7 days later); all patients with single tonic-clonic seizures (before and after the seizures); all patients with syncope (before and after the syncope); and all patients with pseudo-seizures (samples drawn before and after the event). The genes which are examined include but are not limited to: histamine H2-receptor, the c-jun leucine zipper interactive protein, Glut3, the vesicular monoamine transporter, the TNF intracellular domain interacting protein, and the vascular tyrosine phosphatase.

A pattern of expression is captured on an Affymetrix chip. Using an expression method the pattern of expression is defined for single tonic-clonic seizures (before and after the seizures); syncope (before and after the syncope); and pseudo-seizures (samples drawn before and after the event). These patterns are recorded to

develop an injury database for each seizure injury. These injury databases are then used to assess the seizure in an individual.

### **EXAMPLE 8**

This example demonstrates that the pattern of gene expression for each drug is different from each other and different from controls. Blood is obtained from epileptic individuals, epileptic individuals being treated with anticonvulsant valporate and epileptic individuals being treated with anticonvulsant carbamazepine. A pattern of expression is captured and analyzed for each injury state as described in Example 4. As shown in Figure 5, there are some genes upregulated for both anticonvulsants and some genes that are downregulated for both anticonvulsants, but the pattern of expression for each drug is different from each other and different from the controls, the epileptic individuals taking no anticonvulsant.

The data below demonstrates the pattern of expression for valporate and carbamazepine. Table 8a and 8b give lists of genes upregulated or downregulated for valporate, while Tables 8c and 8d give lists of genes upregulated or downregulated for carbamazepine. This data demonstrates how the pattern of expression in the blood of individuals is unique and can be used to assess toxicity or efficacy for a drug or treatment in an individual.

**Table 8a: Upregulated genes for Valporate**

Genbank	Description
M99487	M99487 /FEATURE= /DEFINITION=HUMPSM Human prostate-specific membrane antigen (PSM) mRNA, complete cds
AB023162	Homo sapiens mRNA for KIAA0945 protein, complete cds
X14329	Human mRNA for carboxypeptidase N small subunit (EC 3.4.17.3)
X80907	X80907 /FEATURE= /DEFINITION=HSPHOSINK H.sapiens mRNA for p85 beta subunit of phosphatidyl-inositol-3-kinase
AJ001873	Homo Sapiens mRNA, partial cDNA sequence from cDNA selection, DCR1-16.0
M26683	M26683 /FEATURE= /DEFINITION=HUMIFNIND Human interferon gamma

Genbank	Description
	treatment inducible mRNA
L20861	Homo sapiens proto-oncogene (Wnt-5a) mRNA, complete cds
AF015124	Homo sapiens IgG heavy chain variable region (Vh26) mRNA, partial cds
AI373743	qz54c04.x1 Homo sapiens cDNA, 3 end
AF041339	Homo sapiens homeodomain protein (PITX3) mRNA, complete cds
AF031469	Homo sapiens MHC class I related protein 1 isoform D (MR1D) mRNA, complete cds
AF005361	AF005361 /FEATURE= /DEFINITION=HUMIMPA6 Homo sapiens importin alpha 6 mRNA, complete cds
AB011089	Homo sapiens mRNA for KIAA0517 protein, partial cds
D83407	ZAKI-4 mRNA in human skin fibroblast, complete cds
D83784	Human mRNA for KIAA0198 gene, partial cds
U93917	Human glycine receptor alpha 3 subunit mRNA, complete cds
L05147	Human dual specificity phosphatase tyrosine
M64554	Human factor XIII b subunit gene, complete cds
J03930	Human intestinal alkaline phosphatase (ALPI) gene, complete cds
AL049242	Homo sapiens mRNA; cDNA DKFZp564B083 (from clone DKFZp564B083)
AL022165	dJ71L16.5 (KIAA0267 LIKE putative Na(+))
W27967	40b10 Homo sapiens cDNA
AL109716	Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 208948
AB007913	Homo sapiens mRNA for KIAA0444 protein, partial cds
D32202	Human mRNA for alpha 1C adrenergic receptor isoform 2, complete cds
AF034956	Homo sapiens RAD51D mRNA, complete cds
AF093420	Homo sapiens Hsp70 binding protein HspBP1 mRNA, complete cds
W30959	zc65h10.r1 Homo sapiens cDNA, 5 end
D86640	Homo sapiens mRNA for stac, complete cds
AB020640	Homo sapiens mRNA for KIAA0833 protein, partial cds
U58090	Human Hs-cul-4A mRNA, partial cds
U13022	Human negative regulator of programmed cell death ICH-1S (Ich-1) mRNA, complete cds
S82075	S82075 /FEATURE= /DEFINITION=S82075 PA4=candidate oncogene {3 region} [human, HEN-16, HEN-16T transformed endocervical cell lines, mRNA Partial, 315 nt]
AB025186	Homo sapiens mRNA for EB3 protein, complete cds
U02082	Human guanine nucleotide regulatory protein (tim1) mRNA, complete cds
L15309	Human zinc finger protein (ZNF141) mRNA, complete cds
X83127	H.sapiens mRNA for voltage gated potassium channels, beta subunit
AC004770	Homo sapiens chromosome 11, BAC CIT-HSP-311e8 (BC269730) containing the hFEN1 gene
U83598	U83598 /FEATURE= /DEFINITION=HSU83598 Human death domain receptor 3 soluble form (DDR3) mRNA, partial cds
U81787	U81787 /FEATURE= /DEFINITION=HSU81787 Human Wnt10B mRNA, complete cds
W26334	26b1 Homo sapiens cDNA
AF009242	Homo sapiens proline-rich Gla protein 1 (PRGP1) mRNA, complete cds
AI307607	tb15h10.x1 Homo sapiens cDNA, 3 end

Genbank	Description
M59499	Human lipoprotein-associated coagulation inhibitor (LACI) gene
X96584	H.sapiens mRNA for NOV protein
U71087	U71087 /FEATURE= /DEFINITION=HSU71087 Human MAP kinase kinase MEK5b mRNA, complete cds
M35198	M35198 /FEATURE= /DEFINITION=HUMINTB6A Human integrin B-6 mRNA, complete cds
AF025304	Homo sapiens protein-tyrosine kinase EPHB2v (EPHB2) mRNA, complete cds
AC005053	Homo sapiens BAC clone RG041D11 from 7q21
D17291	Human gene for regenerating protein I beta, complete cds
U28687	Human zinc finger containing protein ZNF157 (ZNF157) mRNA, complete cds
D26535	Human gene for dihydrolipoamide succinyltransferase, complete cds (exon 1-15)
L12760	Human phosphoenolpyruvate carboxykinase (PCK1) gene, complete cds with repeats
U62325	Human FE65-like protein (hFE65L) mRNA, partial cds
AB006624	Homo sapiens mRNA for KIAA0286 gene, partial cds
D14539	Human mRNA for LTG19
U52112	neural cell adhesion molecule L1
AL080140	Homo sapiens mRNA; cDNA DKFZp434L243 (from clone DKFZp434L243)
U19977	Human preprocarboxypeptidase A2 (proCPA2) mRNA, complete cds
AA418437	zv92d11.r1 Homo sapiens cDNA, 5 end
U17579	Human growth hormone-releasing hormone receptor gene, alternatively spliced forms a, b, and c, partial cds
X82634	Homo sapiens mRNA for hair keratin acidic 3-II
AL080175	Homo sapiens mRNA; cDNA DKFZp434K091 (from clone DKFZp434K091)
M20919	Human DNA with a hepatitis B virus surface antigen (HBsAg) gene (complete cds) insertion
AA733050	zg79b05.s1 Homo sapiens cDNA, 3 end
Z78388	HSZ78388 Homo sapiens cDNA
AI819249	wj42f05.x1 Homo sapiens cDNA, 3 end
AB011147	Homo sapiens mRNA for KIAA0575 protein, complete cds
AF097935	Homo sapiens desmoglein 1 (DSG1) mRNA, complete cds
AB004848	Homo sapiens mRNA expressed in placenta, clone IMAGE-70506
P97Antigen,Melanoma-Specific	P97 Antigen, Melanoma-Specific
D87463	Human mRNA for KIAA0273 gene, complete cds
AF052150	Homo sapiens clone 24533 mRNA sequence
M64929	Human protein phosphatase 2A alpha subunit mRNA, complete cds
AF045941	Homo sapiens sciellin (SCEL) mRNA, complete cds
AB028996	Homo sapiens mRNA for KIAA1073 protein, complete cds
M68520	M68520 /FEATURE= /DEFINITION=HUMCDC2A Human cdc2-related protein kinase mRNA, complete cds
Helix-Loop-HelixProteinDeltaMax,Alt.Splice1	Helix-Loop-Helix Protein Delta Max, Alt. Splice 1
AI985019	wu44a10.x1 Homo sapiens cDNA, 3 end

Genbank	Description
AF035314	Homo sapiens clone 23651 mRNA sequence
AB023157	Homo sapiens mRNA for KIAA0940 protein, complete cds
X51630	X51630 /FEATURE=mRNA /DEFINITION=HSWT1 Human Wilms tumor WT1 mRNA for zinc finger protein, Krueppel-like
AB018349	Homo sapiens mRNA for KIAA0806 protein, complete cds
U02632	Human calcium-activated potassium channel mRNA, partial cds
J05096	Human Na,K-ATPase subunit alpha 2 (ATP1A2) gene, complete cds
D79995	Human mRNA for KIAA0173 gene, complete cds
U66582	Human gammaC-crystallin (CRYGC) mRNA, complete cds
U43527	U43527 /FEATURE= /DEFINITION=HSU43527 Human malignant melanoma metastasis-suppressor (KISS-1) gene, mRNA, complete cds
M60299	M60299 /FEATURE=cds /DEFINITION=HUMCOLII Human alpha-1 collagen type II gene, exons 1, 2 and 3
L08488	L08488 /FEATURE= /DEFINITION=HUMINOS Human inositol polyphosphate 1-phosphatase mRNA, complete cds
AL022718	dJ1052M9.3 (mouse DOC4 LIKE protein)
W03846	za60a02.r1 Homo sapiens cDNA, 5 end
AF012130	Homo sapiens brachyury variant A (TBX1) mRNA, complete cds
AF075292	Homo sapiens fibroblast growth factor 18 (FGF18) mRNA, complete cds
D43772	D43772 /FEATURE= /DEFINITION=HUMGRB7 Human squamous cell carcinoma of esophagus mRNA for GRB-7 SH2 domain protein, complete cds
X13967	X13967 /FEATURE=cds /DEFINITION=HSLIF Human mRNA for leukaemia inhibitory factor (LIF/HILDA)
AF041210	Homo sapiens midline 1 fetal kidney isoform 3 (MID1) mRNA, partial cds
	X07876 /FEATURE=cds /DEFINITION=HSIRP Human mRNA for irp protein (int-1 related protein) /NOTE=replacement of probe set 439_at
U76366	Human Treacher Collins syndrome (TCOF1) mRNA, complete cds
RetinoicAcidReceptor,Gamma 2	Retinoic Acid Receptor, Gamma 2
W28161	42h10 Homo sapiens cDNA
X99688	H.sapiens mRNA from TYL gene
W26805	13a12 Homo sapiens cDNA
W26019	18b9 Homo sapiens cDNA
AI828210	wk81e09.x1 Homo sapiens cDNA, 3 end
U79725	Human A33 antigen precursor mRNA, complete cds
AL109722	Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 31619
AB014544	Homo sapiens mRNA for KIAA0644 protein, complete cds
W27763	37c8 Homo sapiens cDNA
D12763	Homo sapiens mRNA for ST2 protein
X84003	H.sapiens TAFII18 mRNA for transcription factor TFIID
S66666	p53=tumor suppressor {alternatively spliced, exon 9-10} [human, Molt-4, T-lymphoblastic leukemia cell line, mRNA PartialMutant, 160 nt]
AF077954	Homo sapiens protein inhibitor of activated STAT protein PIASx-beta mRNA, complete cds
R37702	yf50d02.s1 Homo sapiens cDNA, 3 end
AA418080	zv97h07.s1 Homo sapiens cDNA, 3 end

Genbank	Description
AB028994	Homo sapiens mRNA for KIAA1071 protein, partial cds
Z26308	H.sapiens isoform 1 gene for L-type calcium channel, neuronal subform (partial)
AB003592	Homo sapiens mRNA for neural adhesion molecule NB-3, complete cds
M77348	Human Pmel 17 mRNA, complete cds
U15306	Human cysteine-rich sequence-specific DNA-binding protein NFX1 mRNA, complete cds
AI880840	at11d06.x1 Homo sapiens cDNA, 3 end
AB006651	Homo sapiens EXLM1 mRNA, complete cds
Z19585	Z19585 /FEATURE=cds /DEFINITION=HSTHROMB4 H.sapiens mRNA for thrombospondin-4
U50535	U50535 /FEATURE= /DEFINITION=HSU50535 Human BRCA2 region, mRNA sequence CG006
M85164	Homo sapiens SRF accessory protein 1B (SAP-1) mRNA, complete cds
V01510	H.sapiens gene coding for ACTH and beta-LPH precursors. Gene codes for the common precursor of the pituitary hormones corticotropin (ACTH) and beta-lipotropin (beta-LPH)
U66048	Human clone 161455-2-3 B cell expressed mRNA from chromosome X
AB024729	Homo sapiens hGnT-IV-H mRNA for alpha-1,3-D-mannoside beta-1,4-N-acetylglucosaminyltransferase IV-homologue, complete cds
AJ001634	Homo sapiens mRNA for CC-chemokine MCP-4
AF052186	Homo sapiens clone 24431 mRNA sequence
AF084535	Homo sapiens laforin (EPM2A) mRNA, partial cds
U20982	Human insulin-like growth factor binding protein-4 (IGFBP4) gene, promoter and complete cds
L32164	Homo sapiens zinc finger protein mRNA, 3 end
X16866	X16866 /FEATURE= /DEFINITION=HSP450II Human mRNA for cytochrome P-450IID (clone pMP33)
AJ011733	Homo sapiens mRNA for synaptogyrin 4 protein
X77533	H.sapiens mRNA for activin type II receptor
U16861	Human inward rectifying potassium channel mRNA, complete cds
X99141	H.sapiens mRNA for hair keratin, hHb3
D86962	Human mRNA for KIAA0207 gene, complete cds
AI936759	wp69b12.x1 Homo sapiens cDNA, 3 end
X99947	Homo sapiens mRNA dynein-related protein
AL050287	Homo sapiens mRNA; cDNA DKFZp586C021 (from clone DKFZp586C021)
AF070628	Homo sapiens clone 24803 mRNA sequence
AJ011123	Homo sapiens mRNA for phosphatidylinositol 4-kinase (NPIK-C)

**Table 8b: Downregulated genes for Valporate**

Genbank	Description
AB014514	Homo sapiens mRNA for KIAA0614 protein, partial cds
AF015767	Homo sapiens brain and reproductive organ-expressed protein (BRE) mRNA, complete cds
AF038564	Homo sapiens atrophin-1 interacting protein 4 (AIP4) mRNA, partial cds

Genbank	Description
X62055	X62055 /FEATURE=cds /DEFINITION=HSPTP1C H.sapiens PTP1C mRNA for protein-tyrosine phosphatase 1C
AB001740	Homo sapiens mRNA for p27, complete cds
X16901	Human mRNA for RAP30 subunit of transcription initiation factor RAP30
U10324	Human nuclear factor NF90 mRNA, complete cds
AL022326	dJ333H23.2.2 (Synaptogyrin 1A (SYNGR1A))
AA552988	nk83d08.s1 Homo sapiens cDNA, 3 end
L13616	Human focal adhesion kinase (FAK) mRNA, complete cds
X59656	X59656 /FEATURE=cds /DEFINITION=HSCRKL H.sapiens crk-like gene CRKL
U92817	Homo sapiens unnamed HERV-H protein mRNA, complete cds
X70218	X70218 /FEATURE= /DEFINITION=HSPPX Homo sapiens mRNA for protein phosphatase X
AF030427	Homo sapiens lung type-I cell membrane-associated protein hT1a-1 (hT1a-1) mRNA, complete cds
M37238	M37238 /FEATURE=mRNA /DEFINITION=HUMPLC Human phospholipase C mRNA, complete cds
D11151	D11151 /FEATURE=_expandCDS /DEFINITION=HUMETAR8 Human DNA for endothelin-A receptor, exon 8 and 3 flanking region
AB018258	Homo sapiens mRNA for KIAA0715 protein, partial cds
M69043	M69043 /FEATURE= /DEFINITION=HUMMAD3A Homo sapiens MAD-3 mRNA encoding Ikb-like activity, complete cds
AL050395	Homo sapiens mRNA; cDNA DKFZp586D1020 (from clone DKFZp586D1020)
X73608	H.sapiens mRNA for testican
D26362	Human mRNA for KIAA0043 gene, complete cds
X06318	X06318 /FEATURE=cds /DEFINITION=HSPKCB1A Human mRNA for protein kinase C (PKC) type beta I
R54564	yg81b12.s1 Homo sapiens cDNA, 3 end
D80008	Human mRNA for KIAA0186 gene, complete cds
D88799	D88799 /FEATURE= /DEFINITION=D88799 Homo sapiens mRNA for cadherin, partial cds
U02570	U02570 /FEATURE= /DEFINITION=HSU02570 Human CDC42 GTPase-activating protein mRNA, partial cds
U49392	Human allograft inflammatory factor-1 (AIF-1) mRNA, complete cds
U84894	Human 239AB mRNA, complete cds
Y12851	Homo sapiens P2X7 gene, exon 1 and joined CDS
D42123	Homo sapiens mRNA for ESP1
AF070585	Homo sapiens clone 24675 mRNA sequence

**Table 8c: Upregulated genes for Carbamazepine**

Genbank	Description
AB000824	Homo sapiens mRNA for trehalase, complete cds
AA883870	am26f01.s1 Homo sapiens cDNA, 3 end
L18920	Human MAGE-2 gene exons 1-4, complete cds
Z19585	Z19585 /FEATURE=cds /DEFINITION=HSTHROMB4 H.sapiens mRNA for thrombospondin-4

Genbank	Description
U83410	Human CUL-2 (cul-2) mRNA, complete cds
L34838	Homo sapiens early placenta insulin-like peptide EPIL (INSL4) mRNA, complete cds
U16258	U16258 /FEATURE= /DEFINITION=HSU16258 Human I kappa BR mRNA, complete cds
X02750	Human liver mRNA for protein C
U27516	U27516 /FEATURE= /DEFINITION=HSU27516 Human recombination protein RAD52 mRNA, complete cds
M35296	M35296 /FEATURE= /DEFINITION=HUMARGCAA Human tyrosine kinase arg gene mRNA

**Table 8d: Downregulated genes for Carbamazepine**

Genbank	Description
AB014514	Homo sapiens mRNA for KIAA0614 protein, partial cds
AF015767	Homo sapiens brain and reproductive organ-expressed protein (BRE) mRNA, complete cds
AF038564	Homo sapiens atrophin-1 interacting protein 4 (AIP4) mRNA, partial cds
X62055	X62055 /FEATURE=cds /DEFINITION=HSPTP1C H.sapiens PTP1C mRNA for protein-tyrosine phosphatase 1C
AB001740	Homo sapiens mRNA for p27, complete cds
X16901	Human mRNA for RAP30 subunit of transcription initiation factor RAP30
U10324	Human nuclear factor NF90 mRNA, complete cds
AL022326	dJ333H23.2.2 (Synaptogyrin 1A (SYNGR1A))
AA552988	nk83d08.s1 Homo sapiens cDNA, 3 end
L13616	Human focal adhesion kinase (FAK) mRNA, complete cds
X59656	X59656 /FEATURE=cds /DEFINITION=HSCRKL H.sapiens crk-like gene CRKL
U92817	Homo sapiens unnamed HERV-H protein mRNA, complete cds
X70218	X70218 /FEATURE= /DEFINITION=HSPPX Homo sapiens mRNA for protein phosphatase X
AF030427	Homo sapiens lung type-I cell membrane-associated protein hT1a-1 (hT1a-1) mRNA, complete cds
M37238	M37238 /FEATURE=mRNA /DEFINITION=HUMPLC Human phospholipase C mRNA, complete cds
D11151	D11151 /FEATURE=_expandCDS /DEFINITION=HUMETAR8 Human DNA for endothelin-A receptor, exon 8 and 3 flanking region
AB018258	Homo sapiens mRNA for KIAA0715 protein, partial cds
M69043	M69043 /FEATURE= /DEFINITION=HUMMAD3A Homo sapiens MAD-3 mRNA encoding Ikb-like activity, complete cds
AL050395	Homo sapiens mRNA; cDNA DKFZp586D1020 (from clone DKFZp586D1020)
X73608	H.sapiens mRNA for testican
D26362	Human mRNA for KIAA0043 gene, complete cds
X06318	X06318 /FEATURE=cds /DEFINITION=HSPKCB1A Human mRNA for protein kinase C (PKC) type beta I
R54564	yg81b12.s1 Homo sapiens cDNA, 3 end
D80008	Human mRNA for KIAA0186 gene, complete cds
D88799	D88799 /FEATURE= /DEFINITION=D88799 Homo sapiens mRNA for cadherin,

Genbank	Description
	partial cds
U02570	U02570 /FEATURE= /DEFINITION=HSU02570 Human CDC42 GTPase-activating protein mRNA, partial cds
U49392	Human allograft inflammatory factor-1 (AIF-1) mRNA, complete cds
U84894	Human 239AB mRNA, complete cds
Y12851	Homo sapiens P2X7 gene, exon 1 and joined CDS
D42123	Homo sapiens mRNA for ESP1
AF070585	Homo sapiens clone 24675 mRNA sequence

### **EXAMPLE 9**

This example demonstrates that the pattern of expression for each neurofibromatosis individual as compared to individuals without neurofibromatosis.

- 5 Blood is obtained from neurofibromatosis individuals and individuals without neurofibromatosis. The patterns of expressions are captured and analyzed as described in Example 4. As shown in Figure 6, there is a defined pattern of expression for neurofibromatosis individuals that is different from individuals without neurofibromatosis.

- 10 The data below demonstrates the pattern of expression for neurofibromatosis. Table 9a and 9b give lists of genes upregulated or downregulated for neurofibromatosis. This data demonstrates how the pattern of expression in the blood of individuals is unique and can be used to assess proliferative injury including neurofibromatosis, in an individual.

- 15 **Table 9a: Upregulated genes**

Genbank	Description
M91368	Human Na <sup>+</sup>
Z83838	Human DNA sequence from PAC 127B20 on chromosome 22q11.2-qter, contains gene for GTPase-activating protein similar to rhoGAP protein. ribosomal protein L6 pseudogene, ESTs and CA repeat
V01512	V01512 /FEATURE=mRNA#1 /DEFINITION=HSCFOS Human cellular oncogene c-fos (complete sequence)

Genbank	Description
V01512	V01512 /FEATURE=mRNA#2 /DEFINITION=HSCFOS Human cellular oncogene c-fos (complete sequence)
AI275093	ql65c10.x1 Homo sapiens cDNA, 3 end
AF034633	Homo sapiens orphan G protein-coupled receptor (GPR39) mRNA, complete cds
U59863	Human TRAF-interacting protein I-TRAF mRNA, complete cds
AF011468	Homo sapiens serine
AB014515	Homo sapiens mRNA for KIAA0615 protein, complete cds
M89470	Human paired-box protein (PAX2) mRNA, complete cds
AB011141	Homo sapiens mRNA for KIAA0569 protein, complete cds
U70987	U70987 /FEATURE= /DEFINITION=HSU70987 Human GAP binding protein p62dok (DOK) mRNA, complete cds
M22995	Human ras-related protein (Krev-1) mRNA, complete cds
U55184	Human G protein Golf alpha gene
U81523	Human endometrial bleeding associated factor mRNA, complete cds
S81439	S81439 /FEATURE= /DEFINITION=S81439 EGR alpha=early growth response gene alpha [human, prostate, mRNA, 3228 nt]
D79989	Human mRNA for KIAA0167 gene, complete cds
Y11251	H.sapiens mRNA for novel member of serine-arginine domain protein, SRrp129
AB028956	Homo sapiens mRNA for KIAA1033 protein, partial cds
Z36531	H.sapiens mRNA for fibrinogen-like protein (pT49 protein)
AF078544	Homo sapiens brain mitochondrial carrier protein-1 (BMCP1) mRNA, nuclear gene encoding mitochondrial protein, complete cds
M76446	Human alpha-A1-adrenergic receptor mRNA, complete cds
U04636	U04636 /FEATURE=mRNA /DEFINITION=HSU04636 Human cyclooxygenase-2 (hCox-2) gene, complete cds
X61118	Human TTG-2 mRNA for a cysteine rich protein with LIM motif
K00650	K00650 /FEATURE=cds /DEFINITION=HUMFOS Human fos proto-oncogene (c-fos), complete cds
AB007945	Homo sapiens mRNA for KIAA0476 protein, complete cds
D38524	D38524 /FEATURE= /DEFINITION=HUM5N Human mRNA for 5'-nucleotidase
AB018276	Homo sapiens mRNA for KIAA0733 protein, partial cds
AF088219	Homo sapiens CC chemokine gene cluster, complete sequence
AL008583	dJ327J16.1 (human ortholog of mouse outer arm Dynein light chain 4)
M24283	Human major group rhinovirus receptor (HRV) mRNA, complete cds
AB013382	Homo sapiens mRNA for DUSP6, complete cds
U67322	Human HBV associated factor (XAP4) mRNA, complete cds
U06698	Human neuronal kinesin heavy chain mRNA, complete cds
X03168	Human mRNA for S-protein
X78711	H.sapiens mRNA for glycerol kinase testis specific 1
AF025530	Homo sapiens leucocyte immunoglobulin-like receptor-6a (LIR-6) mRNA, complete cds
AF051426	Homo sapiens slow delayed rectifier channel subunit mRNA, complete cds
U95735	Human SNARE protein Ykt6 (YKT6) mRNA, complete cds
U43519	Human dystrophin-related protein 2 (DRP2) mRNA, complete cds
D80005	Human mRNA for KIAA0183 gene, partial cds
AL050145	Homo sapiens mRNA; cDNA DKFZp586C2020 (from clone DKFZp586C2020)
X51345	Human jun-B mRNA for JUN-B protein
AW005997	wz91c01.x1 Homo sapiens cDNA, 3 end

Genbank	Description
L23805	L23805 /FEATURE= /DEFINITION=HUMCATENIN Human alpha1(E)-catenin mRNA, complete cds
X54637	X54637 /FEATURE=cds /DEFINITION=HSTYK2 Human tyk2 mRNA for non-receptor protein tyrosine kinase
Y11731	H.sapiens mRNA for DNA glycosylase
M76125	M76125 /FEATURE= /DEFINITION=HUMTYRKINR Human tyrosine kinase receptor (axl) mRNA, complete cds
L28957	Homo sapiens CTP-phosphocholine cytidyltransferase mRNA, complete cds
U64520	Human synaptobrevin-3 mRNA, complete cds
AL021808	Human DNA sequence from clone 24o18 on chromosome 6p21.31-22.2 Contains zinc finger protein pseudogene, VNO-type olfactory receptor pseudogene, nuclear envelope pore membrane protein, EST, STS, GSS
X68880	H.sapiens EMX2 mRNA
L29254	Human (clone P1-5) L-itol-2 dehydrogenase gene
AF051323	Homo sapiens Src-associated adaptor protein (SAPS) mRNA, complete cds
M29039	M29039 /FEATURE=cds /DEFINITION=HUMJUNCAA Human transactivator (jun-B) gene, complete cds
AI375610	ta08f06.x1 Homo sapiens cDNA, 3 end
AF060219	Homo sapiens RCC1-like G exchanging factor RLG mRNA, complete cds
S74017	S74017 /FEATURE= /DEFINITION=S74017 Nrf2=NF-E2-like basic leucine zipper transcriptional activator [human, hemin-induced K562 cells, mRNA, 2304 nt]
U01923	Human BTK region clone ftp-3 mRNA
X71874	X71874 /FEATURE=cds#2 /DEFINITION=HSPROSCHY H.sapiens genes for proteasome-like subunit (MECL-1), chymotrypsin-like protease (CTRL-1) and protein serine kinase (PSK-H1) last exon
U03100	Human alpha2(E)-catenin mRNA, complete cds

**Table 9b: Down regulated genes**

Genbank	Description
AF009624	Homo sapiens KIF3-related motor protein (KIF3X) mRNA, partial cds
X97671	X97671 /FEATURE=cds /DEFINITION=HSERYTHR H.sapiens mRNA for erythropoietin receptor
X91348	H.sapiens predicted non coding cDNA (DGCR5)
X68679	H. sapiens mRNA for DOWN 16
Z37986	H.sapiens mRNA for phenylalkylamine binding protein
AF007871	Homo sapiens torsinA (DYT1) mRNA, complete cds
W27191	23e6 Homo sapiens cDNA
Z98265	Homo sapiens mRNA for plakophilin 3
J04132	Human T cell receptor zeta-chain mRNA, complete cds
AA885106	am31h01.s1 Homo sapiens cDNA, 3 end
AL120500	DKFZp761M078_s1 Homo sapiens cDNA, 3 end
D85245	Homo sapiens mRNA for TR3beta, complete cds
U79115	U79115 /FEATURE= /DEFINITION=HSU79115 Human death adaptor molecule RAIDD (RAIDD) mRNA, complete cds
AF048713	Homo sapiens Kv4.3 potassium channel long splice variant (Kv4.3) mRNA, complete cds

Genbank	Description
M64716	Human ribosomal protein S25 mRNA, complete cds
U01038	Human pLk mRNA, complete cds
AF047715	Homo sapiens A-kinase anchoring protein (AKAP18) mRNA, complete cds
U43195	Human Rho-associated, coiled-coil containing protein kinase p160ROCK mRNA, complete cds
U18550	Human GPR3 G protein-coupled receptor gene, complete cds
W28616	49b9 Homo sapiens cDNA
X72631	H.sapiens mRNA encoding Rev-ErbAalpha
AF059198	Homo sapiens protein kinase
J04423	J04423 E coli bioB gene biotin synthetase (-5, -M, -3 represent transcript regions 5 prime, Middle, and 3 prime respectively)
U50535	U50535 /FEATURE= /DEFINITION=HSU50535 Human BRCA2 region, mRNA sequence CG006
U15782	Human cleavage stimulation factor 77kDa subunit mRNA, complete cds
X90872	H.sapiens mRNA for gp25L2 protein
U09577	Homo sapiens lysosomal hyaluronidase (LUCA2
AL049415	Homo sapiens mRNA; cDNA DKFZp586N2119 (from clone DKFZp586N2119)
H16917	ym39e02.r1 Homo sapiens cDNA, 5 end
AB007510	Homo sapiens mRNA for PRP8 protein, complete cds
X03453	X03453 /description=Bacteriophage P1 ORF2, putative cre protein
AI968364	wu02c08.x1 Homo sapiens cDNA, 3 end
AF088219	Homo sapiens CC chemokine gene cluster, complete sequence
J04423	J04423 E coli bioB gene biotin synthetase (-5, -M, -3 represent transcript regions 5 prime, Middle, and 3 prime respectively)
D29805	Human mRNA for beta-1,4-galactosyltransferase, complete cds
X74328	H.sapiens mRNA for CB2 (peripheral) cannabinoid receptor
AF026291	Homo sapiens chaperonin containing t-complex polypeptide 1, delta subunit (Cctd) mRNA, complete cds
Y00097	Human mRNA for protein p68
AI332820	qp96e06.x1 Homo sapiens cDNA, 3 end
X73114	H.sapiens mRNA for slow MyBP-C
U29615	Human chitotriosidase precursor mRNA, complete cds
J04423	J04423 E coli bioB gene biotin synthetase (-5, -M, -3 represent transcript regions 5 prime, Middle, and 3 prime respectively)
Y15801	Homo sapiens mRNA for PRKY protein
AB020706	Homo sapiens mRNA for KIAA0899 protein, partial cds
S69115	granulocyte colony-stimulating factor induced gene [human, CML patient, bone marrow mononuclear cells, mRNA, 833 nt]
U68487	Human 5-hydroxytryptamine7 receptor isoform b mRNA, complete cds
AL109696	Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 21920
AF000571	Homo sapiens kidney and cardiac voltage dependent K+ channel (KvLQT1) mRNA, complete cds
M19309	Human slow skeletal muscle troponin T mRNA, clone H22h
AJ237672	Homo sapiens mRNA for methylenetetrahydrofolate reductase
U80735	Homo sapiens CAGF28 mRNA, partial cds
X04688	X04688 /FEATURE=cds /DEFINITION=HSIL5R Human mRNA for T-cell replacing factor (interleukin-5)
D86956	Human mRNA for KIAA0201 gene, complete cds

Genbank	Description
X58199	Human mRNA for beta adducin
U86214	U86214 /FEATURE= /DEFINITION=HSU86214 Human Fas-associated death domain protein interleukin-1b-converting enzyme 2 mRNA, complete cds
AI553878	tn30a05.x1 Homo sapiens cDNA, 3 end
X90763	Homo sapiens mRNA for type I keratin
AB014535	Homo sapiens mRNA for KIAA0635 protein, complete cds
AJ012611	Homo sapiens mRNA for SIX3 protein
M31651	Homo sapiens sex hormone-binding globulin (SHBG) gene, complete cds
AB028967	Homo sapiens mRNA for KIAA1044 protein, complete cds
X13293	X13293 /FEATURE=cds /DEFINITION=HSBMYB Human mRNA for B-myb gene
J03407	Human rfp transforming protein mRNA, complete cds
D17427	Human mRNA for desmocollin type 4
AL049280	Homo sapiens mRNA; cDNA DKFZp564K143 (from clone DKFZp564K143)
U73394	Human NK-receptor (KIR-103AST) mRNA, complete cds
U67369	Human growth factor independence-1 (Gfi-1) mRNA, complete cds
X91148	H.sapiens mRNA for microsomal triglyceride transfer protein
X97229	H.sapiens mRNA for NK receptor, clone library 15.212
AB014581	Homo sapiens mRNA for KIAA0681 protein, partial cds
M73628	Homo sapiens kappa-casein mRNA, complete cds
AF052145	Homo sapiens clone 24400 mRNA sequence
AF090097	Homo sapiens clone IMAGE 25997
AB023177	Homo sapiens mRNA for KIAA0960 protein, partial cds
X53281	H.sapiens BTF3b mRNA
L78440	L78440 /FEATURE=mRNA /DEFINITION=HUMSTAT4R Homo sapiens STAT4 mRNA, complete cds
U11276	Human hNKR-P1a protein (NKR-P1A) mRNA, complete cds
AB018258	Homo sapiens mRNA for KIAA0715 protein, partial cds
M98539	M98539 /FEATURE=exon /DEFINITION=HUMPDS03 Human prostaglandin D2 synthase gene, exon 7
AL022721	dJ109F14.2 (60S Ribosomal Protein RPL10A)
Rad2	Rad2
AL050152	Homo sapiens mRNA; cDNA DKFZp586K1220 (from clone DKFZp586K1220)
U47025	Human fetal brain glycogen phosphorylase B mRNA, complete cds
AA464312	zx78c11.r1 Homo sapiens cDNA, 5 end
X55954	Human mRNA for HL23 ribosomal protein homologue
X51688	X51688 /FEATURE=mRNA /DEFINITION=HSCYCLINA Human mRNA for cyclin A
U09196	Human 1.1 kb mRNA upregulated in retinoic acid treated HL-60 neutrophilic cells
U08438	Human beta-adrenergic receptor kinase (ADRBK1) gene
X16867	Human mRNA for cytochrome P-450IID (clone pMP34)
U26209	Human renal sodium
X95808	H.sapiens mRNA for protein encoded by a candidate gene, DXS6673E, for mental retardation
AB007895	Homo sapiens KIAA0435 mRNA, complete cds
M21624	M21624 /FEATURE=mRNA /DEFINITION=HUMTCRGC Human T-cell receptor delta chain mRNA (VJC-region), complete cds
AI207842	ao89h09.x1 Homo sapiens cDNA, 3 end
U24266	Human pyrroline-5-carboxylate dehydrogenase (P5CDh) mRNA, long form,

Genbank	Description
	complete cds

#### **EXAMPLE 10**

This example demonstrates that the pattern of expression for each bipolar, manic-depressive, individuals as compared to individuals without bipolar. Blood is obtained from bipolar individuals and individuals without bipolar. The patterns of expressions are captured and analyzed as described in Example 4. As shown in Figure 7, a defined pattern of expression for bipolar individuals is determined that is different from individuals without bipolar.

The data below demonstrates the pattern of expression for bipolar. Table 10a and 10b give lists of genes upregulated or downregulated for bipolar. This data demonstrates how the pattern of expression in the blood of individuals is unique and can be used to assess psychosis, including bipolar, in an individual.

**Table 10a: Upregulated genes**

Genbank	Description
U81787	U81787 /FEATURE= /DEFINITION=HSU81787 Human Wnt10B mRNA, complete cds
AF049498	Homo sapiens sodium channel beta 2 subunit (SCN2B) mRNA, complete cds
M21985	M21985 /FEATURE= /DEFINITION=HUMSRTR2A Human steroid receptor TR2 mRNA, complete cds
AF010403	Homo sapiens ALR mRNA, complete cds
X12794	X12794 /FEATURE=cds /DEFINITION=HSEAR2 Human v-erbA related ear-2 gene
D42046	Human mRNA for KIAA0083 gene, partial cds
AF000987	Homo sapiens eIF-1A, Y isoform (EIF1AY) mRNA, complete cds
M58459	Human ribosomal protein (RPS4Y) isoform mRNA, complete cds
AI208485	qg36f11.x1 Homo sapiens cDNA, 3 end
AF054185	Homo sapiens proteasome subunit HSPC mRNA, complete cds
J05068	human transcobalamin I mRNA, complete cds
L32137	Human germline oligomeric matrix protein (COMP) mRNA, complete cds
X83127	H.sapiens mRNA for voltage gated potassium channels, beta subunit
AL050130	Homo sapiens mRNA; cDNA DKFZp586H051 (from clone DKFZp586H051)
Z97055	Human DNA sequence from PAC 388M5 on chromosome 22. Contains a 60S Ribosomal protein L1 like pseudogene, a chromosomal protein HMG-17 like gene, a Sulfotransferase (Sulfokinase) like gene, a putative GS2 like gene, a predicted CpG island, ESTs and STSs

Genbank	Description
AF034102	Homo sapiens NBMPR-insensitive nucleoside transporter ei (ENT2) mRNA, complete cds
X16666	Human HOX2I mRNA from the Hox2 locus

**Table 10b: Downregulated genes**

Genbank	Description
W80358	zh49a07.s1 Homo sapiens cDNA, 3 end
AF076292	Homo sapiens TGF-beta
X83877	H.sapiens mRNA for ABP
AF083322	Homo sapiens centriole associated protein CEP110 mRNA, complete cds
Y00064	Human mRNA for secretogranin I (chromogranin B)
L26336	Human heat shock protein HSPA2 gene, complete cds
AB011106	Homo sapiens mRNA for KIAA0534 protein, partial cds
S66213	integrin alpha 6B [human, mRNA Partial, 528 nt]
AF093774	Homo sapiens type 2 iodothyronine deiodinase mRNA, complete cds and 3UTR
L41607	Human beta-1,6-N-acetylglucosaminyltransferase (IGnT) gene
Spermidine	Spermidine/Spermine N1-Acetyltransferase, Alt. Splice 2
U43604	Human unidentified mRNA, partial sequence
D00408	D00408 /FEATURE= /DEFINITION=HUMXYPFLA Human fetal liver cytochrome P-450 (P-450 HFLa), complete cds
S68805	L-arginine-glycine amidinotransferase [human, kidney carcinoma cells, mRNA, 2330 nt]
AB020665	Homo sapiens mRNA for KIAA0858 protein, partial cds
AB014593	Homo sapiens mRNA for KIAA0693 protein, partial cds
U13045	Human nuclear respiratory factor-2 subunit beta 1 mRNA, complete cds
J03870	Human cystatin SA-I mRNA, complete cds
U13696	U13696 /FEATURE=cds /DEFINITION=HSU13696 Human homolog of yeast mutL (hPMS2) gene, complete cds
M86407	Homo sapiens alpha actinin 3 (ACTN3) mRNA, complete cds
W25945	17c5 Homo sapiens cDNA
U34962	Human transcription factor HCSX (hCsx) mRNA, complete cds
AF033382	Homo sapiens potassium channel mRNA, complete cds
U45255	Human paired-box protein PAX2 (PAX2) gene
AA767013	oa42a08.s1 Homo sapiens cDNA
W25951	17d10 Homo sapiens cDNA
AF071504	Homo sapiens syntaxin 11 mRNA, complete cds
AB011095	Homo sapiens mRNA for KIAA0523 protein, partial cds
M29874	M29874 /FEATURE= /DEFINITION=HUMCYP2BB Human cytochrome P450-IIB (hIIB1) mRNA, complete cds
L08599	L08599 /FEATURE= /DEFINITION=HUMUVOECAD Human uvomorulin (E-cadherin) (UVO) mRNA, complete cds

### **EXAMPLE 11**

This example demonstrates that the pattern of expression for each individual with acute migraine headaches as compared to individuals without acute migraine headaches. Blood is obtained from individual with acute migraine headaches and individuals without acute migraine headaches. The patterns of expressions are captured and analyzed as described in Example 4. As shown in Figure 8, there is a defined pattern of expression for individual with acute migraine headaches that is different from individual without acute migraine headaches.

The data below demonstrates the pattern of expression for acute migraine headaches. Table 11a and 11b give lists of genes upregulated or downregulated for acute migraine headaches. This data demonstrates how the pattern of expression in the blood of individuals is unique and can be used to assess headaches, including acute migraine headaches, in an individual.

**Table 11a: Upregulated genes**

Genbank	Description
U81523	Human endometrial bleeding associated factor mRNA, complete cds
M91368	Human Na <sup>+</sup>
Y11731	H.sapiens mRNA for DNA glycosylase
AF045581	Homo sapiens BRCA1 associated protein 1 (BAP1) mRNA, complete cds
M94172	Human N-type calcium channel alpha-1 subunit mRNA, complete cds
M60724	Human p70 ribosomal S6 kinase alpha-I mRNA, complete cds
M76125	M76125 /FEATURE= /DEFINITION=HUMTYRKINR Human tyrosine kinase receptor (axl) mRNA, complete cds
AF071538	Homo sapiens Ets transcription factor PDEF (PDEF) mRNA, complete cds
AF019415	untitled
M10098	M10098 Human 18S rRNA gene, complete (_5, _M, _3 represent transcript regions 5 prime, Middle, and 3 prime respectively)
L10403	Homo sapiens DNA binding protein for surfactant protein B mRNA, complete cds
U86813	Homo sapiens serotonin-7 receptor pseudogene, complete sequence
AF005082	Homo sapiens skin-specific protein (xp33) mRNA, partial cds
AF076844	Homo sapiens Hus1-like protein (HUS1) mRNA, complete cds
X59812	X59812 /FEATURE=cds /DEFINITION=HSVD3HYD H.sapiens CYP 27 mRNA for vitamin D3 25-hydroxylase

**Table 11b: Downregulated genes**

Genbank	Description
U79115	U79115 /FEATURE= /DEFINITION=HSU79115 Human death adaptor molecule RAIDD (RAIDD) mRNA, complete cds
X91348	H.sapiens predicted non coding cDNA (DGCR5)
AD001528	Homo sapiens spermidine aminopropyltransferase mRNA, complete cds
W28616	49b9 Homo sapiens cDNA
AA885106	am31h01.s1 Homo sapiens cDNA, 3 end
AF001435	Human clone iota unknown protein mRNA, complete cds
AF007871	Homo sapiens torsinA (DYT1) mRNA, complete cds
D17516	Homo sapiens mRNA for PACAP receptor, complete cds
AL050370	Homo sapiens mRNA; cDNA DKFZp566C0546 (from clone DKFZp566C0546)
AL021026	dJ127D3.2 (Flavin-containing Monooxygenase family protein)
U57721	Human L-kynurenine hydrolase mRNA, complete cds

### EXAMPLE 12

This example demonstrates that the pattern of expression for each individual with schizophrenia as compared to individuals without schizophrenia. Blood is obtained from individual with schizophrenia and individuals without schizophrenia. The patterns of expression are captured and analyzed as described in Example 4. As shown in Figure 9, there is a defined pattern of expression for individual with schizophrenia that is different from individual without schizophrenia.

The data below demonstrates the pattern of expression for schizophrenia. Table 12a and 12b give lists of genes upregulated or downregulated for schizophrenia. This data demonstrates how the pattern of expression in the blood of individuals is unique and can be used to assess schizophrenia in an individual.

**Table 12a: Upregulated genes**

Genbank	Description
Z54367	H.sapiens gene for plectin
D79989	Human mRNA for KIAA0167 gene, complete cds
AF060865	Homo sapiens chromosome 16 zinc finger protein ZNF210 (ZNF210) mRNA, complete cds
X69699	H.sapiens Pax8 mRNA
X80907	X80907 /FEATURE= /DEFINITION=HSPHOSINK H.sapiens mRNA for p85 beta subunit of phosphatidylinositol-3-kinase
D45421	Human mRNA for phosphodiesterase I alpha, complete cds

Genbank	Description
Z83838	Human DNA sequence from PAC 127B20 on chromosome 22q11.2-qter, contains gene for GTPase-activating protein similar to rhoGAP protein. ribosomal protein L6 pseudogene, ESTs and CA repeat
D90239	Human mRNA for glycine decarboxylase
AA203717	zx52f12.r1 Homo sapiens cDNA, 5 end
Z97029	Homo sapiens mRNA for ribonuclease H I large subunit

**Table 12b: Downregulated genes**

Genbank	Description
X02956	X02956 /FEATURE=cds /DEFINITION=HSIFNA5 Human interferon alpha gene IFN-alpha 5
X97630	X97630 /FEATURE= /DEFINITION=HSSTPKEMK H.sapiens mRNA for serine/threonine protein kinase EMK
X75756	X75756 /FEATURE=cds /DEFINITION=HSPKCMU H.sapiens mRNA for protein kinase C mu
D25303	Human mRNA for integrin alpha subunit, complete cds
L36033	Human pre-B cell stimulating factor homologue (SDF1b) mRNA, complete cds
D87440	Human mRNA for KIAA0252 gene, partial cds
M16505	Human steroid sulfatase (STS) mRNA, complete cds
M27533	Human Ig rearranged B7 protein mRNA VC1-region, complete cds
M81652	Homo sapiens semenogelin II mRNA, complete cds
Z97632	dJ196E23.3 (bombesin-like receptor 3 (Bombesin Receptor subtype-3, Uterine Bombesin Receptor, BRS-3))
AL021026	dJ127D3.2 (Flavin-containing Monooxygenase family protein)
X91868	H.sapiens mRNA for SIX1 protein
AF056732	untitled
Insulin-LikeGrowthFactorIb	Insulin-Like Growth Factor Ib
S38742	S38742 /FEATURE= /DEFINITION=S38742 HOX11=HOX11 homeodomain {homeobox} [human, mRNA, 1988 nt]
AJ010901	Homo sapiens MUC4 gene, 3 flanking region
AA156237	zl50c09.s1 Homo sapiens cDNA, 3 end
U85658	Human transcription factor ERF-1 mRNA, complete cds
AI820718	ye38e04.y5 Homo sapiens cDNA, 5 end
X58199	Human mRNA for beta adducin
AB007957	Homo sapiens mRNA, chromosome 1 specific transcript KIAA0488
AJ001875	Homo Sapiens mRNA,partial cDNA sequence from cDNA selection, DCR1-17.0
AI041520	ov82a04.x1 Homo sapiens cDNA, 3 end
Z48054	H.sapiens mRNA for peroxisomal targeting signal 1 (SKL type) receptor
S81661	S81661 /FEATURE= /DEFINITION=S81661 Keratinocyte growth factor [human, mRNA, 1200 nt]
X74331	X74331 /FEATURE=cds /DEFINITION=HSPRIM2 H.sapiens mRNA for DNA primase (subunit p58)
Z93241	dJ222E13.1a.1 (C-terminal part of novel protein dJ222E13.1) (partial isoform 1)
X12654	Human mRNA for cell cycle gene RCC1
X80026	H.sapiens B-cam mRNA

Genbank	Description
D82070	Human aC1 mRNA, complete cds
U04313	U04313 /FEATURE= /DEFINITION=HSU04313 Human maspin mRNA, complete cds
W28846	52g2 Homo sapiens cDNA
AB023194	Homo sapiens mRNA for KIAA0977 protein, complete cds
AF070577	Homo sapiens clone 24461 mRNA sequence
W28876	52h7 Homo sapiens cDNA
AF060503	Homo sapiens zinc finger protein (ZF5128) mRNA, complete cds
M26856	M26856 /FEATURE=cds /DEFINITION=HUMCP21OH Human 21-hydroxylase B gene, complete cds
X63380	Homo sapiens mRNA for serum response factor-related protein, RSRFC2
M88461	Human neuropeptide Y peptide YY receptor mRNA, complete cds
W28438	47g10 Homo sapiens cDNA
W28887	53b4 Homo sapiens cDNA
D25303	D25303 /FEATURE= /DEFINITION=HUMIAS Human mRNA for integrin alpha subunit, complete cds
AF065314	Homo sapiens cone photoreceptor cGMP-gated channel alpha subunit (CNGA3) mRNA, complete cds
AF100780	Homo sapiens connective tissue growth factor related protein WISP-2 (WISP2) mRNA, complete cds
AI824126	wj46e05.x1 Homo sapiens cDNA, 3 end
L36069	Human high conductance inward rectifier potassium channel alpha subunit mRNA, complete cds
D16626	Human mRNA for histidase, complete cds
L20316	Human glucagon receptor mRNA, complete cds
AF076292	Homo sapiens TGF-beta
AL109707	Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 295344
M31525	Human MHC class II lymphocyte antigen (HLA-DNA) gene, complete cds
Y13620	Y13620 /FEATURE= /DEFINITION=HSRNABCL9 Homo sapiens mRNA for BCL9 gene
AB014520	Homo sapiens mRNA for KIAA0620 protein, partial cds
W80358	zh49a07.s1 Homo sapiens cDNA, 3 end
W25951	17d10 Homo sapiens cDNA
S62138	TLS
X15573	Human liver-type 1-phosphofructokinase (PFKL) mRNA, complete cds
AL049261	Homo sapiens mRNA; cDNA DKFZp564E053 (from clone DKFZp564E053)
M16276	Human MHC class II HLA-DR2-Dw12 mRNA DQw1-beta, complete cds
M29874	M29874 /FEATURE= /DEFINITION=HUMCYP2BB Human cytochrome P450-IIB (hIIB1) mRNA, complete cds
AF050078	untitled
AI394290	tg09f06.x1 Homo sapiens cDNA, 3 end
AF004841	Homo sapiens CDO mRNA, complete cds
D23673	Human mRNA, clone HH109 (screened by the monoclonal antibody of insulin receptor substrate-1 (IRS-1))
AJ132445	Homo sapiens CLDN14 gene
Z11584	H.sapiens mRNA for NuMA protein
AC002398	Human DNA from chromosome 19-specific cosmid F25965, genomic sequence

### **EXAMPLE 13**

This example demonstrates that the pattern of expression for each individual with Tourettes as compared to individuals without Tourettes. Blood is obtained from individual with Tourettes and individuals without Tourettes. The patterns of expressions are captured and analyzed as described in Example 4. As shown in Figure 10, there is a defined pattern of expression for individual with Tourettes that is different from individual without Tourettes.

The data below demonstrates the pattern of expression for Tourettes. Table 13a and 13b give lists of genes upregulated or downregulated for Tourettes. This data demonstrates how the pattern of expression in the blood of individuals is unique and can be used to assess Tourettes in an individual.

**Table 13a: Upregulated genes**

Genbank	Description
AI218431	qh24d10.x1 Homo sapiens cDNA, 3 end
AW043925	wy82b07.x1 Homo sapiens cDNA, 3 end
Y17673	Homo sapiens mRNA for nebulin, incomplete splice variant, partial
X07495	Human mRNA for cp19 homeobox from HOX-3 locus
W27997	43e3 Homo sapiens cDNA
AI347129	tc04a03.x1 Homo sapiens cDNA, 3 end
U39576	Human butyrophilin precursor mRNA, complete cds
AF051160	Homo sapiens tyrosine phosphatase (PRL-1) gene, complete cds
U77968	Human neuronal PAS1 (NPAS1) mRNA, complete cds
AJ132337	Homo sapiens mRNA for chemokine receptor CCR9
U07620	U07620 /FEATURE= /DEFINITION=HSU07620 Human MAP kinase mRNA, complete cds

**Table 13b: Downregulated genes**

Genbank	Description
X54637	X54637 /FEATURE=cds /DEFINITION=HSTYK2 Human tyk2 mRNA for non-receptor protein tyrosine kinase
U53204	Human plectin (PLEC1) mRNA, complete cds
AB014587	Homo sapiens mRNA for KIAA0687 protein, partial cds
U31525	Human glycogenin mRNA, complete cds
D38251	Homo sapiens mRNA for RPB5 (XAP4), complete cds

Genbank	Description
D14663	Human mRNA for KIAA0107 gene, complete cds
J05448	J05448 /FEATURE= /DEFINITION=HMRPOLAA Human RNA polymerase subunit hRPB 33, mRNA
X52773	X52773 /FEATURE=cds /DEFINITION=HSRARLP Human mRNA for retinoic acid receptor-like protein
U52840	Homo sapiens semaphorin F homolog mRNA, complete cds
AB002311	Human mRNA for KIAA0313 gene, complete cds
AI796048	wh41g06.x1 Homo sapiens cDNA, 3 end
D10202	D10202 /FEATURE= /DEFINITION=HUMPAFRE Homo sapiens mRNA for platelet-activating factor receptor, complete cds
U22055	Human 100 kDa coactivator mRNA, complete cds
U73704	Homo sapiens 48 kDa FKBP-associated protein FAP48 mRNA, complete cds
L13291	Human ADP-ribosylarginine hydrolase mRNA, complete cds
AF067139	Homo sapiens NADH-ubiquinone oxidoreductase NDUFS3 subunit mRNA, nuclear gene encoding mitochondrial protein, complete cds
AF038203	Homo sapiens clone 23596 mRNA sequence
AB023181	Homo sapiens mRNA for KIAA0964 protein, complete cds
AI864120	wg64a06.x1 Homo sapiens cDNA, 3 end
AC002544	Homo sapiens Chromosome 16 BAC clone CIT987SK-A-761H5
X75621	Homo sapiens TSC2 mRNA for tuberin
M30938	M30938 /FEATURE=mRNA#2 /DEFINITION=HUMKUP Human Ku (p70/p80) subunit mRNA, complete cds
AI417075	tg78e09.x1 Homo sapiens cDNA, 3 end
AL035447	Human DNA sequence from clone 1183I21 on chromosome 20q12. Contains a novel gene and the first exon of a putative novel gene for a protein similar to predicted fly and worm proteins. Contains ESTs, STSs, GSSs and a putative CpG island
U72936	U72936 /FEATURE= /DEFINITION=HSU72936 Homo sapiens putative DNA dependent ATPase and helicase (ATRX) mRNA, alternatively spliced product 1, complete cds
U08997	Human glutamate dehydrogenase gene, complete cds
AF055479	Homo sapiens lung cancer candidate FUS1 (FUS1) mRNA, complete cds
AF070523	Homo sapiens JWA protein mRNA, complete cds
M11058	Human 3-hydroxy-3-methylglutaryl coenzyme A reductase mRNA, complete cds
U19969	Human two-handed zinc finger protein ZEB mRNA, partial cds
X02344	Homo sapiens beta 2 gene
D34625	Human TBXAS1 gene for thromboxane synthase, promoter region and
M60721	M60721 /FEATURE=mRNA /DEFINITION=HUMHB24 Human homeobox gene, complete cds
X76488	H.sapiens mRNA for lysosomal acid lipase
AL031781	dJ51J12.1.3 (human ortholog of mouse KH Domain RNA Binding protein QKI-7 (isoform 3)
U82939	Homo sapiens p53 binding protein mRNA, complete cds
U96074	Human translation initiation factor eIF3 p44 subunit mRNA, complete cds
X65784	H.sapiens CAR gene
W30677	zb75h10.r1 Homo sapiens cDNA, 5 end
U47077	Human DNA-dependent protein kinase catalytic subunit (DNA-PKcs) mRNA, complete cds
M32373	Human arylsulfatase B (ASB) mRNA, complete cds
M34175	Human beta adaptin mRNA, complete cds
U90313	U90313 /FEATURE= /DEFINITION=HSU90313 Human glutathione-S-transferase homolog mRNA, complete cds
AI683748	tw53e07.x1 Homo sapiens cDNA, 3 end
AB014603	Homo sapiens mRNA for KIAA0703 protein, complete cds

Genbank	Description
AF089814	Homo sapiens growth suppressor related (DOC-1R) mRNA, complete cds
AB007960	chromosome 1 specific transcript KIAA0491
M28393	Human perforin mRNA, complete cds
X84709	H.sapiens mRNA for mediator of receptor-induced toxicity
AB014536	Homo sapiens mRNA for KIAA0636 protein, complete cds
L36870	Homo sapiens MAP kinase kinase 4 (MKK4) mRNA, complete cds
AL080144	Homo sapiens mRNA; cDNA DKFZp434N093 (from clone DKFZp434N093)
Z78324	HSZ78324 Homo sapiens cDNA
AF052111	Homo sapiens clone 23953 mRNA sequence
AB002354	Human mRNA for KIAA0356 gene, complete cds
AI436567	ti03b09.x1 Homo sapiens cDNA, 3 end
AF042385	Homo sapiens cyclophilin-33A (CYP-33) mRNA, complete cds
Z25821	H.sapiens gene for mitochondrial dodecenoyl-CoA delta-isomerase, exons 1 and 2
U94778	Human PEST phosphatase interacting protein homolog (H-PIP) mRNA, complete cds
L13435	Human chromosome 3p21.1 gene sequence
M22898	M22898 /FEATURE=mRNA /DEFINITION=HUMP53A11 Human phosphoprotein p53 gene exon 11
J05070	Human type IV collagenase mRNA, complete cds
U47634	U47634 /FEATURE= /DEFINITION=HSU47634 Human beta-tubulin class III isotype (beta-3) mRNA, complete cds
X99906	Homo sapiens mRNA for alpha endosulfine
AF051850	Homo sapiens supervillin mRNA, complete cds
AC002400	Human Chromosome 16 BAC clone CIT987SK-A-735G6
AB028951	Homo sapiens mRNA for KIAA1028 protein, partial cds
Y09538	H.sapiens mRNA for ZNF185 gene
AF041259	Homo sapiens breast cancer putative transcription factor (ZABC1) mRNA, complete cds
L13972	Homo sapiens beta-galactoside alpha-2,3-sialyltransferase (SIAT4A) mRNA, complete cds
X87344	H.sapiens DMA, DMB, HLA-Z1, IPP2, LMP2, TAP1, LMP7, TAP2, DOB, DQB2 and RING8 9, 13 and 14 genes
W28299	44h4 Homo sapiens cDNA
X53390	Human mRNA for upstream binding factor (hUBF)
AI189287	qd05c04.x1 Homo sapiens cDNA, 3 end
L34587	L34587 /FEATURE= /DEFINITION=HUMRPIE Homo sapiens RNA polymerase II elongation factor SIII, p15 subunit mRNA, complete cds
D13146	D13146 /FEATURE=mRNA#1 /DEFINITION=HUM3CNP3 Homo sapiens gene for 2 ,3 -cyclic-nucleotide 3 -phosphodiesterase, exon 3 and complete cds
AB018348	Homo sapiens mRNA for KIAA0805 protein, partial cds
AF052155	Homo sapiens clone 24761 mRNA sequence
S74017	S74017 /FEATURE= /DEFINITION=S74017 Nrf2=NF-E2-like basic leucine zipper transcriptional activator [human, hemin-induced K562 cells, mRNA, 2304 nt]
D87127	D87127 /FEATURE= /DEFINITION=D87127 Homo sapiens mRNA for translocation protein-1, complete cds
U70063	U70063 /FEATURE= /DEFINITION=HSU70063 Human acid ceramidase mRNA, complete cds
Tubulin,Beta2	Tubulin, Beta 2
AF075599	Homo sapiens ubiquitin conjugating enzyme 12 (UBC12) mRNA, complete cds
U80184	Homo sapiens FLII gene, complete cds
U89505	Human Hlark mRNA, complete cds
AF031647	Homo sapiens JAB1-containing signalosome subunit 3 (SGN3) mRNA, complete cds
D83664	Human mRNA for CAAF1 (calcium-binding protein in amniotic fluid 1), complete cds

Genbank	Description
AA457029	aa38b10.s1 Homo sapiens cDNA, 3 end
AL044599	DKFZp434N192_s1 Homo sapiens cDNA, 3 end
X06409	Human mRNA fragment for activated c-raf-1 (exons 8-17)
ProteinKinase Ht31,Camp-Dependent	Protein Kinase Ht31, Camp-Dependent
U79270	Human clone 23707 mRNA, partial cds
AF097358	Homo sapiens mast cell function-associated antigen homolog (MAFA) mRNA, complete cds
Glucocorticoid Receptor,Beta	Glucocorticoid Receptor, Beta
M68864	Human ORF mRNA, complete cds
U15655	Human ets domain protein ERF mRNA, complete cds
Y00281	Human mRNA for ribophorin I
X95762	H.sapiens mRNA for aminopeptidase P-like
U83115	Human non-lens beta gamma-crystallin like protein (AIM1) mRNA, partial cds
D87450	Human mRNA for KIAA0261 gene, partial cds
U17989	Homo sapiens nuclear autoantigen GS2NA mRNA, complete cds
D26535	Human gene for dihydrolipoamide succinyltransferase, complete cds (exon 1-15)
D12686	D12686 /FEATURE= /DEFINITION=HUMEIF4G Human mRNA for eukaryotic initiation factor 4 gamma (eIF-4 gamma)
AF098799	Homo sapiens RanBP7
U18334	U18334 /FEATURE=cds /DEFINITION=HSUNOSIIC1 Human nitric oxide synthase II (NOSIIc) gene, partial exon 23
D87444	Human mRNA for KIAA0255 gene, complete cds
AA576724	nm81b04.s1 Homo sapiens cDNA, 3 end
U79282	Human clone 23801 mRNA sequence
AL050369	Homo sapiens mRNA; cDNA DKFZp566J153 (from clone DKFZp566J153)
D13540	D13540 /FEATURE= /DEFINITION=HUMSHPTP3 Homo sapiens SH-PTP3 mRNA for protein-tyrosine phosphatase, complete cds
X12433	Human pHS1-2 mRNA with ORF homologous to membrane receptor proteins
AB028948	Homo sapiens mRNA for KIAA1025 protein, partial cds
D12620	D12620 /FEATURE= /DEFINITION=HUMCYT1 Homo sapiens mRNA for cytochrome P-450LTBV, complete cds
X91504	H.sapiens mRNA for ARP1 protein
W16505	zb05e12.r1 Homo sapiens cDNA, 5 end
D29677	Human mRNA for KIAA0054 gene, complete cds
AI540318	tq34f03.x1 Homo sapiens cDNA, 3 end
S69189	peroxisomal acyl-coenzyme A oxidase [human, liver, mRNA, 3086 nt]
AB003177	AB003177 /FEATURE= /DEFINITION=AB003177 Homo sapiens mRNA for proteasome subunit p27, complete cds
Z84718	Z84718 /FEATURE=cds#5 /DEFINITION=HS322B1 Human DNA sequence from clone 322B1 on chromosome 22q11-12, complete sequence [Homo sapiens]
AW005997	wz91c01.x1 Homo sapiens cDNA, 3 end
AJ237839	Homo sapiens mRNA for hypothetical protein
U82277	Human immunoglobulin-like transcript 1b mRNA, complete cds
S46950	adenosine A2 receptor [human, hippocampal, mRNA, 2572 nt]
AA478904	zv20c05.r1 Homo sapiens cDNA, 5 end
X71440	H.sapiens mRNA for peroxisomal acyl-CoA oxidase
AI557064	PT2.1_13_A12.r Homo sapiens cDNA, 3 end

Genbank	Description
AB006202	Homo sapiens mRNA for cytochrome b small subunit of complex II, complete cds
AD000092	AD000092 /FEATURE=cds#2 /DEFINITION=CH19HHR23 Homo sapiens DNA from chromosome 19p13.2 cosmids R31240, R30272 and R28549 containing the EKLF, GCDH, CRTC, and RAD23A genes, genomic sequence
	X85545 /FEATURE=cds /DEFINITION=HSPKX1MR H.sapiens mRNA for protein kinase, PKX1 /NOTE=replacement of probe set 132 at
AF047185	Homo sapiens NADH-ubiquinone oxidoreductase subunit CI-B8 mRNA, complete cds
AF104421	Homo sapiens isolate normal patient 1 uroporphyrinogen decarboxylase (UROD) mRNA, complete cds
X98253	H.sapiens ZNF183 gene
Ubiquitin-Conjugating Enzyme Ubch5	Ubiquitin-Conjugating Enzyme Ubch5
AI670788	tz10c02.x1 Homo sapiens cDNA, 3 end
AB017551	Homo sapiens mRNA for 16G2, complete cds
M80359	Human protein p78 mRNA, complete cds
U26710	Human cbl-b mRNA, complete cds
U27460	Human uridine diphosphoglucose pyrophosphorylase mRNA, complete cds
AI347155	tc04c11.x1 Homo sapiens cDNA, 3 end
AL023657	Homo sapiens SH2D1A cDNA, formerly known as DSHP
AF038564	Homo sapiens atrophin-1 interacting protein 4 (AIP4) mRNA, partial cds
Y07604	H.sapiens mRNA for nucleoside-diphosphate kinase
U76247	Human hSIAH1 mRNA, complete cds
M96803	Human general beta-spectrin (SPTBN1) mRNA, complete cds
Z69043	H.sapiens mRNA translocon-associated protein delta subunit precursor
U07158	Human syntaxin mRNA, complete cds
AL078641	Human DNA sequence from clone 494G10 on chromosome 22 Contains part of a gene similar to phorbol 2, ESTs and a GSS
M29551	Human calcineurin A2 mRNA, complete cds
AF042083	Homo sapiens BH3 interacting domain death agonist (BID) mRNA, complete cds
L32977	Homo sapiens (clone f17252) ubiquinol cytochrome c reductase Rieske iron-sulphur protein (UQCRC1) gene
AF059681	Homo sapiens serine
M76231	Human sepiapterin reductase mRNA, complete cds
AL031427	dJ167A19.3 (novel protein)
AI935146	wp14b12.x1 Homo sapiens cDNA, 3 end
AF093771	Homo sapiens mitoxantrone resistance protein 1 mRNA, partial sequence
U79267	Human clone 23840 mRNA, partial cds
M28439	M28439 /FEATURE=cds /DEFINITION=HUMKER16A8 Human keratin type 16 gene, exon 8
AF000364	Homo sapiens heterogeneous nuclear ribonucleoprotein R mRNA, complete cds
D82351	Human retropseudogene MSSP-1 DNA, complete cds
M28212	M28212 /FEATURE= /DEFINITION=HUMRAB6A Homo sapiens GTP-binding protein (RAB6) mRNA, complete cds
AJ236885	Homo sapiens mRNA for ZBP-89 protein
U79291	Human clone 23721 mRNA sequence
AF015926	Homo sapiens ezrin-radixin-moesin binding phosphoprotein-50 mRNA, complete cds
AL050087	Homo sapiens mRNA; cDNA DKFZp434O031 (from clone DKFZp434O031)
AF038952	Homo sapiens cofactor A protein mRNA, complete cds
AC002073	Human PAC clone DJ515N1 from 22q11.2-q22

Genbank	Description
L15388	L15388 /FEATURE= /DEFINITION=HUMGRK5A Human G protein-coupled receptor kinase (GRK5) mRNA, complete cds
L23134	Homo sapiens metase (MET-1) mRNA, complete cds
D42087	Human mRNA for KIAA0118 gene, partial cds
AL049324	Homo sapiens mRNA; cDNA DKFZp564D246 (from clone DKFZp564D246)
U63717	U63717 /FEATURE= /DEFINITION=HSU63717 Homo sapiens osteoclast stimulating factor mRNA, complete cds
AB011113	Homo sapiens mRNA for KIAA0541 protein, partial cds
D00860	Homo sapiens mRNA for phosphoribosyl pyrophosphate synthetase subunit I, complete cds
D82348	Homo sapiens mRNA for 5-aminoimidazole-4-carboxamide-1-beta-D-ribose nucleotide transformylase
D31766	Human mRNA for KIAA0060 gene, complete cds
L13858	Human guanine nucleotide exchange factor mRNA, complete cds
AA151716	zo30d07.s1 Homo sapiens cDNA, 3 end
AF019083	Homo sapiens phosphatase and tensin homolog 2 (PTN2) mRNA, partial cds
AF017445	Homo sapiens GDP-L-fucose pyrophosphorylase (GFPP) mRNA, complete cds
AF038186	Homo sapiens clone 23914 mRNA sequence
AB018257	Homo sapiens mRNA for KIAA0714 protein, partial cds
AF049891	Homo sapiens tyrosylprotein sulfotransferase-2 mRNA, complete cds
AF052186	Homo sapiens clone 24431 mRNA sequence
AF070582	Homo sapiens clone 24766 mRNA sequence
AF055020	Homo sapiens clone 24722 unknown mRNA, partial cds
AF052138	Homo sapiens clone 23718 mRNA sequence
AB000468	Homo sapiens mRNA for zinc finger protein, complete cds, clone-RES4-26
M31158	Human cAMP-dependent protein kinase subunit RII-beta mRNA, complete cds
AB002360	Human mRNA for KIAA0362 gene, partial cds
AB018285	Homo sapiens mRNA for KIAA0742 protein, partial cds
AF013759	Homo sapiens calumenin (Calu) mRNA, complete cds
D87292	Homo sapiens mRNA for rhodanese, complete cds
AB023143	Homo sapiens mRNA for KIAA0926 protein, complete cds
AA194159	zr37h01.r1 Homo sapiens cDNA, 5 end
M96824	Human nucleobindin precursor mRNA, complete cds
X78925	H.sapiens HZF2 mRNA for zinc finger protein
D25235	Human mRNA for alpha1C adrenergic receptor, complete cds
M62896	Human lipocortin (LIP) 2 pseudogene mRNA, complete cds-like region
AB000712	Homo sapiens hCPE-R mRNA for CPE-receptor, complete cds
U26648	Homo sapiens syntaxin 5 mRNA, complete cds
M99439	Human transducin-like enhancer protein (TLE4) mRNA, 3 end
L42450	Homo sapiens pyruvate dehydrogenase kinase isoenzyme 1 (PDK1) mRNA, complete cds
AA913812	ol39a08.s1 Homo sapiens cDNA, 3 end
U29185	Homo sapiens prion protein (PrP) gene, complete cds
Y14768	Homo sapiens DNA, cosmid clones TN62 and TN82
L20321	L20321 /FEATURE= /DEFINITION=HUMSTK2A Human protein serine/threonine kinase stk2 mRNA, complete cds
M28130	M28130 /FEATURE=mRNA /DEFINITION=HUMIL8A Human interleukin 8 (IL8) gene, complete cds
AB018312	Homo sapiens mRNA for KIAA0769 protein, complete cds
U56833	U56833 /FEATURE= /DEFINITION=HSU56833 Human VHL binding protein-1 (VBP-1) mRNA, partial cds

Genbank	Description
U59435	Human cell cycle protein p38-2G4 homolog (hG4-1) mRNA, complete cds
AB018319	Homo sapiens mRNA for KIAA0776 protein, partial cds
AB002381	Human mRNA for KIAA0383 gene, partial cds
M22632	Human mitochondrial aspartate aminotransferase mRNA, complete cds
AA521060	aa71e09.s1 Homo sapiens cDNA, 3 end
AB015051	Homo sapiens mRNA for Daxx, complete cds
Y07846	H.sapiens mRNA for GAR22 protein
AF023612	Homo sapiens Dim1p homolog mRNA, complete cds
D31883	Human mRNA for KIAA0059 gene, complete cds
U89896	Homo sapiens casein kinase I gamma 2 mRNA, complete cds
X15949	X15949 /FEATURE=cds /DEFINITION=HSIRF2 Human mRNA for interferon regulatory factor-2 (IRF-2)
AB028980	Homo sapiens mRNA for KIAA1057 protein, partial cds
L42324	L42324 /FEATURE=cds /DEFINITION=HUMFRCG Homo sapiens (clone GPCR W) G protein-linked receptor gene (GPCR) gene, 5' end of cds
AB023229	Homo sapiens mRNA for KIAA1012 protein, complete cds
AB020636	Homo sapiens mRNA for KIAA0829 protein, partial cds
D86970	Human mRNA for KIAA0216 gene, complete cds
U01923	Human BTK region clone ftp-3 mRNA
U51007	Human 26S protease subunit S5a mRNA, complete cds
M25322	Human granule membrane protein-140 mRNA, complete cds
S76638	S76638 /FEATURE= /DEFINITION=S76638 p50-NF-kappa B homolog [human, peripheral blood T cells, mRNA, 3113 nt]
U60325	U60325 /FEATURE= /DEFINITION=HSU60325 Human DNA polymerase gamma mRNA, nuclear gene encoding mitochondrial protein, complete cds
U91316	Human acyl-CoA thioester hydrolase mRNA, complete cds
L08069	L08069 /FEATURE= /DEFINITION=HUMDNAJHOM Human heat shock protein, E. coli DnaJ homologue mRNA, complete cds
S63912	D10S102=FBRNP [human, fetal brain, mRNA, 3043 nt]
D86062	Human mRNA for KNP-Ib, complete cds
M98343	Homo sapiens amplexin (EMS1) mRNA, complete cds
D13315	Human mRNA for lactoyl glutathione lyase
AB018276	Homo sapiens mRNA for KIAA0733 protein, partial cds
X75346	X75346 /FEATURE=cds /DEFINITION=HSMAPKAP H.sapiens mRNA for MAP kinase activated protein kinase
M28215	Homo sapiens GTP-binding protein (RAB5) mRNA, complete cds
M60784	Human U1 snRNP-specific protein A gene
AB007900	Homo sapiens KIAA0440 mRNA, partial cds
U91512	Human adhesion molecule ninjurin mRNA, complete cds
AF000982	Homo sapiens dead box, X isoform (DBX) mRNA, alternative transcript 2, complete cds
M12267	Human ornithine aminotransferase mRNA, complete cds
D11094	Human mRNA for MSS1, complete cds
U79260	Human clone 23745 mRNA, complete cds
X55079	Human lysosomal alpha-glucosidase gene exon 1
D83782	Human mRNA for KIAA0199 gene, partial cds
R38263	yc92c11.s1 Homo sapiens cDNA, 3 end
M12125	Human fibroblast muscle-type tropomyosin mRNA, complete cds
AB007869	Homo sapiens KIAA0409 mRNA, partial cds
U82130	U82130 /FEATURE= /DEFINITION=HSU82130 Human tumor susceptibility protein (TSG101) mRNA, complete cds

Genbank	Description
U40763	Human Clk-associated RS cyclophilin CARS-Cyp mRNA, complete cds
W94101	ze11c11.r1 Homo sapiens cDNA, 5 end
AA877795	nr10g08.s1 Homo sapiens cDNA, 3 end
AL049442	Homo sapiens mRNA; cDNA DKFZp586N1720 (from clone DKFZp586N1720)
AJ223183	Homo sapiens mRNA for DORA protein
X53587	X53587 /FEATURE=mRNA /DEFINITION=HSINTB4R Human mRNA for integrin beta 4
X99720	H.sapiens TPRC gene
AL050282	Homo sapiens mRNA; cDNA DKFZp586H2219 (from clone DKFZp586H2219)
AA135683	zl10c08.r1 Homo sapiens cDNA, 5 end
AB002369	Human mRNA for KIAA0371 gene, complete cds
AB014562	Homo sapiens mRNA for KIAA0662 protein, partial cds
AA928996	oo27f06.s1 Homo sapiens cDNA, 3 end
AJ132917	Homo sapiens mRNA for methyl-CpG-binding protein 2
W27419	31a10 Homo sapiens cDNA
AL009179	dJ97D16.6 (Histone H3.1)
AF004430	Homo sapiens hD54+ins2 isoform (hD54) mRNA, complete cds
D13627	Human mRNA for KIAA0002 gene, complete cds
D78514	D78514 /FEATURE=cds /DEFINITION=D78514 Homo sapiens mRNA for ubiquitin-conjugating enzyme, complete cds
D14812	Human mRNA for KIAA0026 gene, complete cds
H15872	ym22b12.r1 Homo sapiens cDNA, 5 end
U84971	Homo sapiens fetal unknown mRNA, complete cds
AF040707	Homo sapiens candidate tumor suppressor gene 21 protein isoform I mRNA, complete cds
AL009179	dJ97D16.4 (Histone H2B)
U05875	Human clone pSK1 interferon gamma receptor accessory factor-1 (AF-1) mRNA, complete cds
AC004262	Homo sapiens chromosome 19, cosmid R29368
X77909	H.sapiens IKBL mRNA
D89678	Homo sapiens mRNA for A+U-rich element RNA binding factor, complete cds
AF070533	Homo sapiens clone 24619 mRNA sequence
X04412	Human mRNA for plasma gelsolin
U37547	Human IAP homolog B (MIHB) mRNA, complete cds
AL050157	Homo sapiens mRNA; cDNA DKFZp586O0120 (from clone DKFZp586O0120)
U09825	Human acid finger protein mRNA, complete cds

The specific embodiments and examples set forth above are provided for illustrative purposes only and are not intended to limit the scope of the following claims. Additional embodiments of the invention and advantages provided thereby will be apparent to one of ordinary skill in the art and are within the scope of the claims.